Naval Aerospace Medical Research Laboratory

NAMRL Monograph 38

April 1989

BETA-BLOCKERS:

AN ABSTRACTED BIBLIOGRAPHY

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Reviewed and approved 4 April 1989

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No 0704-0188

1a REPORT SECURITY CLASSIFICATION	1b RESTRICTIVE MARKINGS
2a SECURITY CLASSIFICATION AUTHORITY Unclassified	3 DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release; distribution unlimited.
2b DECLASSIFICATION / DOWNGRADING SCHEDULE	
4 PERFORMING ORGANIZATION REPORT NUMBER(S) NAMRL Monograph 38	5 MONITORING ORGANIZATION REPORT NUMBER(S)
6a NAME OF PERFORMING ORGANIZATION Naval Aerospace Medical Research Laboratory 6b OFFICE SYMBOL (If applicable) 21	7a NAME OF MONITORING ORGANIZATION Naval Medical Research and Development Command
6c ADDRESS (City, State, and ZIP Code) Naval Air Station Pensacola, FL 32508-5700	7b ADDRESS (City, State, and ZIP Code) Naval Medical Command National Capital Region Bethesda, MD 20814-5044
8a NAME OF FUNDING / SPONSORING ORGANIZATION NMRDC 8b OFFICE SYMBOL (If applicable) CODE 404	9 PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c ADDRESS (City, State, and ZIP Code) Commanding Officer, NMRDC, Naval Medical Command, National Capital Region, Bethesda, MD 20814-5044	10 SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO: 61153N PROJECT NO: MR04101 TASK NO: .03 WORK UNIT ACCESSION NO: DN245510

11 TITLE (Include Security Classification)

(U) Beta-blockers: An Abstracted Bibliography

12 PERSONAL AUTHOR(S)

Morey, W. A., Lentz, J. M., and Olafson, R. P.

13a TYPE OF REPORT	13b TIME COVERED	14 DATE OF REPORT (Year, Month, Day)	15 PAGE COUNT
Interim	FROM TO	1989 04 04	68

16 SUPPLEMENTARY NOTATION

17 COSATI CODES			18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB GROUP	Auditory	Blood pressure	Heart rate
			Beta-Blocker	Complex Performance	Histology
			Biochemistry	Exercise	Musculoskeletal (Cont'd.)

19 ABSTRACT (Continue on reverse if necessary and identify by block number)

The bibliographic abstracts in this report are part of a project to assess biomedical effects of beta blockers, which play an important role in the control of hypertension. Specific attention has been focused on the biomedical effects in several general areas: vision, auditory, spatial orientation, musculoskeletal, cardiopulmonary, cognitive performance, pharmacology, cutaneous stimuli, and cortical effects. These investigations, combined with clinical research reports and the experience of our senior flight surgeons, will establish the foundation for judging the potential impact of any specific drug on safety of flight and operational readiness.

20 DISTRIBUTION / AVAILABILITY OF ABSTRACT ☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT ☐ DTIC USERS	21 ABSTRACT SECURITY CLASSIFICATION Unclassified
22a NAME OF RESPONSIBLE INDIVIDUAL J. A. BRADY, CAPT MSC USN, Commanding Officer	22b TELEPHONE (Include A (904) 452-328. OFFICE SYMBOL 00

SUBJECT TERMS (Cont'd.)

Neuroelectric	Review	Vision
Pharmacology	Stress	
Psychology	Ventilation	

Accession For	
NTIS GRA&I	☑
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Unannounced	☐
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A-1	

PREFACE

The Naval Aerospace Medical Research Laboratory is engaged in an effort to determine the effects on performance of several commonly used therapeutic drugs. These investigations, combined with clinical research reports and the experience of our senior flight surgeons, establish the foundation for judging the potential impact of any specific drug treatment on safety of flight and operational readiness. This bibliography focuses on a group of drugs called beta-blockers, which play an important role in the control of hypertension. The abstracted bibliography is designed as a working document reflecting a literature search and establishes the basic material for a literature summary.

We have chosen a printing format, tear-out 5 x 8 index cards, to reflect our emphasis on producing a versatile working document, which can be supplemented with future abstracts. A topic-area index is provided at the end of the monograph. The topic area descriptions for each abstract can be found at the bottom of each 5 x 8 card and represent three general areas: drug, (each specified drug is listed), biomedical discipline (general topic area of the report), and subject population (human or nonhuman).

A numerical filing system can be found at the top right side of each 5 x 8 card. The numerical system corresponds to an alphabetical order by author. This initial volume uses numerical intervals of 10, which will allow abstracts from future volumes to be merged while still retaining a numerical and alphabetical order. Only English language articles or those with an English-language summary are included.

Each abstract contains eight sections of information: Authors, Title, Reference, Drugs (including dosages when feasible), Subjects (number and type), Procedures (brief general description), Findings (brief listing of major findings), and Index (the topic-area index). In some cases, it was necessary to use more than one 5 x 8 card to adequately abstract the article.

ACKNOWLEDGMENTS

The development of this abstracted bibliography was greatly facilitated by the assistance of Ruth Rodgers and Ann Chalk in the Naval Aerospace Medical Institute Library.

We would also like to acknowledge the invaluable assistance provided by Ensign Daniel K. Shields, and Mrs. Elaine Cotton and Mrs. Nell Davis who typed and prepared the manuscript. We would also like to thank DPI Sharon Winter for assistance with the word processing program. Our appreciation is also extended to Kathleen Mayer and Dr. Fred Guedry, Jr., for editorial comments.

AUTHORS: Abdel-Latif, A. A.

TITLE: Effects of Neurotransmitters and Neuropharmacological Agents on Phospholipid Metabolism in the Rabbit Iris Muscle.

REFERENCE: Advances in Experimental Medicine and Biology, Vol. 72, pp. 227-256, 1976.

DRUGS: Eserine
dl-Propranolol
Sotalol
Norepinephrine (NE)
Acetylcholine (ACh)
Atropine

SUBJECT: Rabbit iris muscle

PROCEDURE: Labeling study on incubated mixtures containing the iris muscle.

FINDINGS:
Acetylcholine increased the ^{32}p labeling of Phosphatidic acid (140-205%) and Phosphatidylinositol (175%-229%). Acetylcholine stimulation was blocked by atropine. Eserine had no effect on the ^{32}p labeling. Sotalol exerted no effect on the norepinephrine-stimulated phospholipid labeling. dl-Propranolol did not block the NE-stimulated phospholipid, however, at 0.3mM concentration, it increased the ^{32}p labeling of PhA (10 times) and PhI (2 times).

INDEX: Sotalol, Propranolol, Atropine, Eserine, ACh, Histology, Vision, Nonhuman.

AUTHORS: Allen, J. A., Jenkison, D. J., and Roddie, I. C.

TITLE: The Effect of Beta-adrenergic Blockade on Human Sweating.

REFERENCE: British Journal of Pharmacology, Vol. 47, pp. 487-497, 1972.

DRUGS: Propranolol (0.15 mg/kg, i. v.)
Atropine (2.4 mg, i. v.)

SUBJECTS: 5 young healthy medical students

PROCEDURE: Subjects were placed in an environmental chamber and were continously monitored for total loss of body weight as an index of sweating. Temperatures were set at 29°, 34° and 40° C. Propranolol was administered via an indwelling cannula. Sweating was induced in normal subjects by raising the environmental temperature or by subjecting the subjects to emotional stress or mental arithmetic.

FINDINGS.
Propranolol had no effect on either thermal or emotional sweating. Thermal sweating was blocked temporarily by administration of atropine. Conclusion: Beta-adrenergic blockade had no physiologic effect on sweating in normal individuals.

INDEX: Propranolol, Atropine, Sweating, Human.

30

AUTHORS: Ambrosio, G. B., Benussi, P., Trevi, G. P., and Pessina, A. C.

TITLE: Maximal Exercise Test in Patients with Essential Hypertension Treated with Propranolol.

REFERENCE: European Journal of Cardiology, Vol. 7, pp. 137-145, 1978.

DRUGS: Propranolol

SUBJECTS: Patients (with hypertension)

PROCEDURES: A maximum exercise test using a stationary bicycle ergometer was administered to 15 patients with essential hypertension before and after 10 d of oral propranolol (320 mg, daily).

FINDINGS:
Post-treatment systolic and diastolic blood pressure and heart rate fell dramatically, both at rest and after the exercise. Results indicated a marked reduction in ECG ischemic changes. "Propranolol treatment, besides being an effective antihypertensive agent, improved ischemic changes induced by exercise and cardiac performance in hypertensive patients, also in the presence of left ventricular hypertrophy." There was a significant reduction in the product of heart rate times systolic blood pressure, which is a reliable index of myocardial O_2 consumption.

INDEX: Propranolol, Exercise, HR, BP, Human.

40

AUTHORS: Anderson, S. D., Bye, P. T. P., Perry, C. P., Hamor, G. P., Theobald, G., and Nyberg, G.

TITLE: Limitation of Work Performance in Normal Adult Males in the Presence of Beta-adrenergic Blockade.

REFERENCE Australian and New Zealand Journal of Medicine, Vol. 9, pp. 515-520, 1979.

DRUGS: Metoprolol (100 mg)
Propranolol (80 mg)

SUBJECTS: 10 healthy nonsmoking male volunteers, ages 23-38

PROCEDURES: The effects of exercise following a single dose of metoprolol was compared with effects following an equipotent dose of the propranolol. Several biochemical and physiological parameters including heart rate, oxygen consumption, ventilation, lactate, free fatty acid, and glucose levels were measured.

FINDINGS:
After exercise with each drug, subjects complained of excessive leg fatigue. There was a marked reduction in the total work performed and maximum heart rate and a positive correlation between plasma metoprolol and reduction in heart rate. By contrast, with propranolol there was a wide variation in work performed, although reduction in maximum heart rate was similar for all subjects suggesting that a reduction in heart rate alone is an inappropriate guide to the impairment of work performance. With both drugs, there was a post-exercise fall in plasma fatty acids, which may have contributed to the decrease in work performance.

INDEX: Metoprolol, Propranolol, Exercise, HR, BP, Biochemistry, Human.

50

AUTHORS: Andren, L., Hansson, L., and Bjorkman, M.

TITLE: Haemodynamic Effects of Noise Exposure Before and After Beta-selective Non-selective Beta-adrenoceptor Blockade.

REFERENCE: Clinical Science, Vol. 61, pp. 89-91, 1981.

DRUGS: Metoprolol (0.2 mg/kg)
Propranolol (0.1 mg/kg)

SUBJECTS: 9 male patients with mild or moderate hypertension

PROCEDURES: Noise stimulation (100 dBA For 10 min). Blood pressure was measured indirectly in the brachial artery with an automatic recorder.

FINDINGS:
Noise stimulation caused a significant increase in diastolic and mean arterial blood pressure in patients with essential hypertension. The blood pressure response to noise was due to an increase in total peripheral resistance; heart rate, stroke volume, and cardiac output were unchanged. Metoprolol did not change the hemodynamic reaction pattern induced by noise. Propranolol caused an accentuated blood pressure response with increments of both systolic and diastolic blood pressure and a pronounced rise in total peripheral resistance.

INDEX: Metoprolol, Propranolol, BP, HR, Auditory, Human.

60

AUTHORS: Aronow, W. S., Spivack, N., Laverty, W., and Warren, M.

TITLE: Effect of Tolamolol and Propranolol on Exercise Heart Rate and Angina.

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 17, pp. 379-384, 1975.

DRUGS: Propranolol (10 mg, i.v.)
Tolamolol (10 and 20 mg, i.v.)

SUBJECTS: 15 patients with angina pectoris

PROCEDURES: Monitored HR and BP during angina, exercise, and rest.

FINDINGS:
In equal doses, propranolol was more effective than tolamolol in decreasing (a) resting heart rate, (b) heart rate after exercise, (c) heart rate at the onset of angina, (d) the product of resting systolic pressure times heart rate, and (e) product of systolic pressure times heart rate at the onset of angina. There appeared to be no significant difference between the effect of intravenous administration of 10 mg of tolamolol, 20 mg of tolamolol, or 10 mg of propranolol on the mean onset time of angina. Propranolol produced more than a 25% increase in exercise time preceding onset of angina in 4 of the 15 patients. The article emphasized that the potency ratios after intravenous administration of different beta-adrenergic blocking drugs may be very different from those following oral administration and that acute hemodynamic and anti-anginal effects of beta-adrenergic blocking drugs may differ from those after chronic administration. Also, the maximum anti-anginal effects can be obtained only after titrating the dose of drug used in exercise performance studies.

INDEX: Tolamolol, Propanolol, HR, BP, Exercise, Human.

AUTHOR: Astrand, P. O., Ekblom, B., and Goldbarg, A. N.

TITLE: Effects of Blocking the Autonomic Nervous System During Exercise.

REFERENCE: Acta Physiological Scandinavica, Vol. 82, p. 18-A, 1971.

DRUGS: Propranolol (10 mg, i.v.)
Atropine (2.5 mg, i.v.)

SUBJECT 14 subjects

PROCEDURE: Max VO_2, Ve, and heart rate. Exercise on a bicycle.

FINDING:
Maximum VO_2 decreased 6% after both drugs were used in combination. Neither drug individually affected Max VO_2; however, during max exercise, the time to exhaustion was reduced by propranolol. Resting and submax VO_2 were not affected by either of the drugs separately or together. At rest, atropine increased the heart rate 60%, but this effect became less pronounced as load increased so that the max heart rate was unchanged. Propranolol decreased resting heart rate 6 beats/min and max heart rate by 36 beats/min. The two drugs in combination increased the resting heart rate to normal at 25% of VO_2 max, the effect progessively decreased as max VO_2 was approached.

INDEX: Propranolol, Atropine, HR, BP, Exercise, Human.

AUTHORS: Baird, I. M., Hill, H., Ings, R. M. J., Johnson, K. I., and McEwen, J.

TITLE Dynamic and Kinetic Comparison of Penbutolol in Healthy Volunteers.

reference: British Journal of Clinical Pharmacology, Vol. 4, pp. 386, 1977.

DRUGS:

Propranolol	(160 mg)	and Penbutolol	(40 mg)
"	(80 mg)	"	(20 mg)
"	(40 mg)	"	(10 mg)

SUBJECT: 6 healthy volunteers

PROCEDURE: Pulse rates were recorded at 15-s intervals. Exercise was conducted on a bicycle ergometer. Dose response curves were established for both drugs.

FINDINGS:
The maximum pulse for propranolol was at 2 h and for penbutolol at 1 h. Significant tachycardia could still be detected with either drug at 24 h.

INDEX: Propranolol, Penbutolol, HR, BP, Exercise, Human

AUTHORS: Baldwa, V. S., Gupta, B. S., and Chittora, M. D.

TITLE: Cardiovascular Response to Isometric Stress (Handgrip) in Patients with Essential Hypertension Before and After Antihypertensive Therapy with Propranolol or Alpha Methyldopa.

REFERENCE: Indian Heart Journal, Vol. 35, pp. 333-336, 1983.

DRUGS: Propranolol (80-240 mg/d)
Methyldopa (500-2000 mg/d)

SUBJECTS: 50 patients with hypertension, ages 25-65

PROCEDURES: Maximal voluntary contraction (MVC-handgrip) was recorded for each subject using a hand dynamometer. Each subject was asked to maintain 30% of MVC for at least 3 min, and thereafter as long as one could tolerate. Blood pressure was measured by sphygmomanometer.

FINDINGS:
The response to exercise in hypertensive patients was exaggerated with delayed recovery. Static work index (exercise capacity) was reduced in hypertensives. Antihypertensive therapy reduced the rise of the cardiovascular responses with a gradual build-up, lower ceiling, and rapid rate of recovery. The absolute rise in heart rate, systolic and diastolic BP, and rate-pressure product during isometric stress were significantly lower with propranolol therapy as compared to methyldopa. Rate of recovery was more rapid with propranolol. The difference between drugs in stress reduction responses was explained by different mechanisms of action.

INDEX: Propranolol, Methyldopa, HR, BP, Exercise, Human.

AUTHORS: Banks, D. C., Patrick, J. M., and Pearson, S. B.

TITLE: The Effects of Propranolol and Metoprolol and Exercise Responses in Normal Man.

REFERENCE: British Journal of Clinical Pharmacology, Vol. 6, p. 443P, 1978

DRUGS: Propranolol (80 mg oral single dose)
Metoprolol (100 mg oral single dose)

SUBJECTS: 9 normal men

PROCEDURES: The effect of single doses of the above drugs on the cardiovascular and respiratory responses to bicycle ergometer exercise (to exhaustion) were measured using O_2 in a double-blind protocol. Measurements of fO_2 and O_2 were taken.

FINDINGS:
Both drugs produced a fall in O_2 consumption across the work range. Carbon Dioxide production and ventilation were essentially unchanged. Both compounds produced a rise in the perceived amount of exertion and comparison of actual workload to O_2 consumption.

INDEX: Propranolol, Metoprolol, HR, Exercise, Ventilation, Human.

AUTHORS: Barger, E. M., Walle, U. K., Bai, S. A., and Walle, T.

TITLE: Quantitative Metabolic Fate of Propranolol in the Dog, Rat, and Hamster using Radiotracer, High Performance Liquid Chromatography, and Gas Chromatography.

REFERENCE: Drug Metabolism and Disposition, Vol. 11, pp. 226-272, 1983.

DRUGS: Propranolol

SUBJECTS: Dogs, rats, and hamsters

PROCEDURES: The purpose of this investigation was to develop an analytical method for the separation and measurement of the major propranolol metabolites. A combination of techniques was used to analyze the urine of dogs, rats and hamsters. Labeled and non-labeled propranolol was administered to dogs (po) and to rats and hamsters (i.p.).

FINDINGS:
Liquid scintillation spectrometry and GS/MS allowed for the identification and quantification of 15 phase I metabolites of propranolol. The predominate means of metabolism in the dog was by glucoronidation and oxidation of the side-chain. Ring oxidation was the main means of metabolism in the rat and hamster. There were some metabolites which could not be identified and they appeared to have an elimination which was much slower than that of the drug itself; these could be important if they possess biological activity.

INDEX: Propranolol, Biochemistry, Nonhuman.

AUTHORS: Becker, A. L.

TITLE: Oxprenol and Propranolol in Anxiety States

REFERENCE: South African Medical Journal, Vol. 50, pp. 626-627, 1976.

DRUGS: Propranolol and Oxprenolol

SUBJECTS: 46 patients suffering from anxiety

PROCEDURES: A double-blind study was conducted to evaluate the abilities of the two compounds to control chronic anxiety and tension. Effectiveness was measured by a psychiatric rating scale plus investigator and patient evaluations. Drug tolerance was estimated by a checklist of signs and symptoms.

FINDINGS:
Efficacy of the two drugs was reported to be almost the same and both were effective at controlling tension and anxiety. Oxprenolol was better tolerated by patients. Propranolol had a greater cardiac-depressant effect. Propranolol had significantly more side effects: acathisia, nasal congestion, diarrhea, bradycardia, drowiness, hypotension, constipation, nausea/vomiting, and dizziness/faintness/weakness.

INDEX: Propranolol, Oxprenol, Questionnaire, Human.

AUTHORS: Bjurstedt, H., Rosenhamer, G., and Tyden, G.

TITLE: Acceleration Stress and Effects of Propranolol on Cardiovascular Responses.

REFERENCE: Acta Physiologica Scandinavica, Vol. 90, pp. 491-500, 1974.

DRUGS: Propranolol (0.25 mg/kg b.wt.)

SUBJECTS: 6 physically well-trained, young male volunteers

PROCEDURES: Heart rate, arterial pressure, and cardiac output were recorded in the sitting position at normal gravity and at 3 G acting in the head-seat direction, before and after beta-adrenergic blockade. Studies were performed both at rest and during leg exercise.

FINDINGS:
After propranolol, the heart rate response to increased G at rest averaged 38% of that observed without blockade. G-induced cardiac output decline was more marked after propranolol, this effect being entirely due to the reduced response of the heart rate. In spite of the cardioinhibitory effects of propranolol, subjective G-force tolerance was well preserved; the response of the arterial mean pressure to increased G was unaffected due to a 65% rise in systemic vascular resistance as against 43% before propranolol. Hence, sympathetic chronotropic stimulation of the heart is not essential for the circulatory defense against increased G stress. Transition from rest to exercise at 3 G produced a larger increase in stroke volume than in heart rate; after propranolol, the dominance of the stroke volume enhancement was exaggerated.

INDEX: Propranolol, HR, BP, Exercise, G-Tolerance, Human.

AUTHORS: Boutellier, U. and Koller, E. A.

TITLE: Propranolol and the Respiratory, Circulatory, and EEG Response to High Altitude.

REFERENCE: European Journal of Applied Physiology, Vol. 46, pp. 105-119, 1981.

DRUGS: Propranolol (80,60,40 mg)

SUBJECTS: 20 adult volunteers

PROCEDURES: The study was designed to investigate the role of the sympathoadrenal system in the acute respiratory and cardiovascular responses to high altitude (6000 m in a low pressure chamber) with and without propranolol. Emphasis focused on ECG change induced by hypoxia.

FINDINGS:
"Propranolol beneficially acted to reduce the amount of hypoxia-induced ECG changes. At altitude, ECG changes during myocardic depolorization occurred in both the propranolol and the control groups, probably due to the direct effects of hypoxia. During the repolorization phase, propranolol led to an almost complete abolition of S-T depression and to significant reduction of T-wave flattening."

INDEX: Propranolol, HR, Ventilation, Human.

AUTHORS: Brick, I., Glover, W. E., Hutchison, K. J., and Boddie, I. C.

TITLE: Effects of Propranolol on Peripheral Vessels in Man.

REFERENCE: American Journal of Cardiology, Vol. 18, pp. 329-332, 1966.

DRUGS: Propranolol (10 ug/min), Norepinephrine (0.5 ug/min), Isoproterenol (0.25 ug/min), Histamine (5 ug/min), Epinephrine (1.0 ug/min)

SUBJECTS: Healthy male subjects

PROCEDURES: Two series of experiments were performed on subjects in the supine position. Blood flow was measured by venous occlusion plethysmography. Drugs were administered via indwelling catheter (one brachial artery), or by IV infusion. Heart rate and blood pressure were recorded.

FINDINGS:
Propranolol effectively blocked the vasodilator or beta-adrenergic activity of the catecholamines in the forearm. Thus, the usual vasodilator effect of isoproterenol when given either I.V. or I.A. was abolished. The biphasic response to I.A. epinephrine was converted into a purely constrictor one, and post-infusion dilatation was abolished. The response to I.V. epinephrine was converted into a constrictor one. The response to both I.V. and I.A. norepinephrine was unchanged in these experiments. The I.A. experiments showed slight attenuation of the vasodilation induced by histamine while treated with propranolol.

INDEX: Propranolol, Norepinephrine, Isoproterenol, Histamine, Epinephrine, HR, BP, Human.

AUTHORS: Broadhurst, A. D.

TITLE: Comparison of Effect on Psychomotor Performance of Single Doses of Propranolol and Acebutolol.

REFERENCE: Current Medical Research Opinion, Col. 7, pp. 33-37, 1980.

DRUGS: Propranolol (40 mg)
Acebutolol (100 mg)

SUBJECTS: 10 healthy male volunteers

PROCEDURES: Subjects were given single doses of propranolol and acebutolol orally, using a double-blind placebo-controlled design. Psychomotor function was assessed by means of a Random Stimulus Generator/Complex Reaction Timer. Measures included visual and auditory simple reaction time, vigilance, discrimination, and accuracy.

FINDINGS:
Complex reaction time was slowed by propranolol. Acebutolol did not produce a slowing of reaction time.

INDEX: Propranolol, Acebutolol, Complex Performance, Vision, Auditory, Human.

AUTHORS: Broadhurst, A. D.

TITLE: The Effect of Propranolol on Human Psychomotor Performance.

REFERENCE: Aviation Space and Environmental Medicine, Vol. 51, pp. 176-179, 1980.

DRUGS: Propranolol (40-120 mg/day)
Amylobarbitone (25-50 mg)

SUBJECTS: 8 men and 2 women, ages 21-38

PROCEDURES: Psychomotor function was measured by means of a Random Stimulus Generator/Complex Reaction Timer.

FINDINGS:
Even a single 40-mg dose of propranolol produced a significant slowing of the response time. In chronic administration (3 weeks), there was a marked recovery of reaction time.

INDEX: Propranolol, Amylobarbitone, Complex Performance, Human.

AUTHORS: Broadhurst, A. D. and Monaghan, A. T.

TITLE: The Effect of Single Doses of Penbutolol and Propranolol LA on Psychomotor Performance.

REFERENCE: British Journal of Clinical Pharmacology, Vol. 17, pp. 591-594, 1984.

DRUGS: Propranolol (160 mg)
Penbutolol (40 mg)

SUBJECTS: 12 normal subjects

PROCEDURES: Psychomotor performance effects of propranolol and penbutolol assessed using a double-blind, three-part (propranolol, penbutolol and placebo) cross-over design. Psychomotor effects were evaluated using a Random Stimulus Generator/Complex Reaction Timer, which measured visual and auditory reaction time, vigilance, discrimination, and accuracy.

FINDINGS:
Propranolol produced muzziness in one subject. Penbutolol caused some nausea, muzziness, and drowsiness. At 3 h post administration, both penbutolol and propranolol significantly increased complex reaction times; at 24 hours this effect had worn-off.

INDEX: Propranolol, Penbutolol, Complex Performance, Human.

AUTHORS: Bruce, R. A., Hossack, K. F., Kusumi, F., and Clarke, L. J.

TITLE: Acute Effects of Oral Propranolol on Hemodynamic Responses to Upright Exercise.

REFERENCE: American Journal of Cardiology, Vol. 44, pp. 132-140, 1979.

DRUGS: Propranolol (40 mg)

SUBJECTS: 3 healthy men and 14 men with coronary heart disease

PROCEDURES: Noninvasive measurement of maximum oxygen intake, invasive measurement of systemic and pulmonary arterial pressures, arterial and mixed venous oxygen contents, and direct Flick cardiac output are reported.

FINDINGS:
The most persistent effect of propranolol was reduction of pressure-rate products at all phases; slowing of heart rate was significant only during exercise and recovery, and greater slowing was accompanied by a significant increase in stroke volume. Maximum oxygen intake decreased in healthy subjects and decreased slighty in patients with coronary heart disease with less than 15% left ventricular impairment or percentage deviation of pressure-rate product from age-related normal values during the control study. Maximum oxygen intake increased in patients with more than 15% left ventricular impairment.

INDEX: Propranolol, HR, BP, Ventilation, Human.

AUTHORS: Burhring, M., Kemmerer, K., and Kappos, A.

TITLE: Cardiovascular and Respiratory Function Values in Hyperthermia: The Effect of Beta-receptor Blockade with Bunitrolol.

REFERENCE: Klinische Wochenschnft, Vol. 60, pp. 617-623, 1982.

DRUGS: Bunitrolol (10 mg, o.p.)

SUBJECTS: 12 healthy men, ages 21-29

PROCEDURES: Cardiovascular parameters and oscillatory respiratory resistance were investigated in response to hyperthermia.

FINDINGS:
There was no change in the tachycardiac response to hyperthermia (warm bath) following bunitrolol. In some patients, there was a feeling of general distress, restlessness, nervous excitement, and motor agitation (an increase of such emotions is characteristic of heat stroke).

INDEX Bunitrolol, HR, BP, Heat Stress, Human.

AUTHORS: Chasiotis, D., Brandt, P., Harris, C., and Hultman, E.

TITLE: Effects of Beta-blockade on Glycogen Metabolism in Human Subjects During Exercise.

REFERENCE: American Journal of Physiology, Vol. 245, pp. 166-170, 1983.

DRUGS: Propranolol (5 mg) in 5 ml saline infused for 5 min into the left cubital vein. Infusion was repeated after 20-30 min rest.

SUBJECTS: 18 healthy volunteers (8 males and 10 females), ages 17-37, normal body weight

PROCEDURES: Isometric exercise and dynamic exercise. Muscle biopsy samples were taken at rest and immediately after termination of exercise, for determination of cAMP, hexosemonophosphates, lactate, phosphorylase, synthetase 1, and glycogen.

FINDINGS:
The cAMP content of the muscle was unchanged by isometric exercise, but dynamic exercise doubled it. The cAMP content at rest was reduced by propranolol and did not increase during subsequent exercise. Hexosemonophosphates normally increased six-fold with exercise but not after administration of propranolol. The accumulation of lactic acid was slighty reduced by propranolol. During exercise with propranolol, phosphorylase 'a' decreased more than normal, whereas, there was no effect on synthetase 1. Beta-blockade had no effect on muscle glycogenolysis during isometric contraction but decreased the rate of glycogen degradation during dynamic exercise.

INDEX: Propranolol, Exercise, Histology, Human.

AUTHORS: Coleman, J. H.

TITLE: Concepts in Beta Blockade.

REFERENCE: Diseases of the Nervous System, Vol. 36, pp. 46-47, 1975.

DRUGS: Propranolol

SUBJECTS: N/A

PROCEDURES: Review paper

FINDINGS:
The report is a brief review of concepts in the use of beta-blockade, mainly discussing the uses of propranolol. It concludes that propranolol is a pharmacologically pure beta-adrenergic antagonist without other autonomic activity. The article discusses other uses of the drug: (1) treatment of tremors of familial, senile or essential types, (2) treatment of the peripheral manifestations of thyrotoxicosis, and (3) control of anxiety syndrome associated with sedative-hypnotic withdrawal. Propranolol use should be carefully monitored when administered in combination with other pharmaceuticals.

INDEX: Propranolol, Review, Human.

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AUTHORS: Cooke, J. N. C.

TITLE: Chairman's Opening Remarks and General Panel Discussion.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 53, pp. 346-548, 1981.

DRUGS: Beta-blockers in general.

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
Hypertension has long been identified as one of the three major risk factors for ischemic heart disease and probably the major factor for cardiovascular disease. It has assumed a considerable importance as a finding in the routine examination of flight deck crew, pilots, and air traffic controllers. Beta-blockade has become the most widely used form of treatment for hypertension in the U.K., and is now the agent of first choice of many clinicians. There are a number of possible advantages in its use in aircrew, including the alteration of cardiovascular responses to emotional stress.

INDEX: Propranolol, Review, Human.

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AUTHORS: Cremona-Barbaro, A.

TITLE: Propranolol and Depression.

REFERENCE: Lancet, Vol. 1, p. 185, 1983.

DRUGS: Propranolol (10 mg, twice daily)

SUBJECTS: One 63-year-old female and one 62-year-old man

PROCEDURES: NA

FINDINGS:
The female patient had previous depression and was prescribed propranolol 10 mg twice daily for hypertension and became seriously depressed. The male patient also had been previously depressed. He was taking 10 mg propranolol three times a day for hypertension. Within 2 weeks after starting medication, he began to complain of severe depression. When both patients discontinued propranolol, the depression immediately began to resolve.

INDEX: Propranolol, Psychology, Human.

AUTHORS: Cruickshank, K., Neil-Dwyer, G., Cameron, M. M., and McAinsh, J.

TITLE: Beta-adrenoreceptor-blocking Agents and the Blood Brain Barrier.

REFERENCE: Clinical Science, Vol. 59, pp. 453-455, 1980.

DRUGS: Propranolol (80 mg twice daily)
Metoprolol (100 mg twice daily)
Atenolol (100 mg twice daily)

SUBJECTS: 9 patients (8 with a subarachnoid haemorrhage at least 1 week before and 1 patient with back pain) 7 patients (5 with aneurysm, 2 with depression).

PROCEDURES: Cerebrospinal fluid and plasma assays.

FINDINGS:
The lipophilic beta-receptor blockers, propranolol and metoprolol, appeared in cerebrospinal fluid at concentrations similar to the free drug plasma concentrations in brain tissue (about 20 times lower than the lipophilic beta-receptor blocker); the brain/plasma ratio was approximately 0.1:1. Central nervous system-related effects associated with propranolol and metoprolol appear to be the result of high brain tissue concentrations.

INDEX: Propranolol, Metoprolol, Histology, Human.

AUTHORS: Dollery, C. T., Bulpitt, C. J., Daniel, J., and Clifton, P.

TITLE: Eye Symptoms in Patients Taking Propranolol and Other Hypotensive Agents.

REFERENCE: British Journal of Clinical Pharmacology, Vol. 4, pp. 295-297, 1977.

DRUGS: Propranolol and other hypertensive drugs.

SUBJECTS: 483 hypertensive patients treated with propranolol or other hypotensive drugs

PROCEDURES: Questionnaire.

FINDINGS:
The questions were deliberately composed to keep the complaint rate low by using the word often and by confining the complaint to the recent past (last 3 months). Even so, approximately 25% of the patients gave a response indicating a corneal problem or a problem with photophobia (gritty feelings in eyes, sore eyes, red eyes, bright lights hurt eyes, and used eyedrops).

INDEX: Propranolol, Questionnaire, Vision, Human.

AUTHORS: Dunn, F. G., Lorimer, A. R., and Lawrie, T. D. V.

TITLE: Objective Measurement of Performance During Acute Stress in Patients with Essential Hypertension: Assessment of the Effects of Propranolol and Metoprolol.

REFERENCE: Clinical Science, Vol. 57, pp. 413-415, 1979.

DRUGS: Propranolol (single dose)
Metoprolol (single dose)

SUBJECTS: 18 patients (17 males and 1 female) with idiopathic hypertension

PROCEDURES: A car-driving simulator with auditory and visual stimuli. Heart rate and blood pressure were recorded.

FINDINGS:
Baseline heart rate fell from a mean of 91 to 71 beats/min with propranolol and from 88 to 67 with metoprolol. A significant rise in heart rate occurred during the driving test regardless of the presence of the drug. There was a 6% rise in heart rate with propranolol and a 10% rise without it, and there was a 6% rise with metoprolol and a 13% rise without it. The rise in blood pressure in response to the test was less with the blockers but not significantly so.

INDEX: Propranolol, Metoprolol, HR, BP, Stress, Human.

AUTHORS: Ekblom, B., Goldbarg, A. N., Kilbom, A., and Astrand, P. O.

TITLE: Effects of Atropine and Propranolol on the Oxygen Transport System During Exercise in Man.

REFERENCE: Scandinavian Journal of Clinical and Laboratory Investigation, Vol. 30, pp. 35-42, 1972.

DRUGS: Atropine (2.0-2.5 mg, i.v.)
Propranolol (10 mg, i.v.)

SUBJECTS: 14 healthy male subjects (non-athletes)

PROCEDURES: Subjects performed submaximal and maximal bicycle exercise under control and drug conditions.

FINDINGS:
The lowest heart rate was noticed after propranolol. The average heart rate with propranolol was about 40 beats/min less than that following atropine. The maximal oxygen uptake was unchanged except after the combined drug administration when there was a 6% reduction. Maximal work time and cardiac output were significantly reduced by propranolol. A remarkably efficient arterial oxygen transport can be maintained during heavy exercise despite a wide variation in heart rate.

INDEX: Atropine, Propranolol, Exercise, HR, Ventilation, Human.

290

AUTHORS: Eliasch, H., Rosen, A., and Scott, H. M.

TITLE: Systemic Circulatory Response to Stress of Simulated Flight and to Physical Exercise Before and After Propranolol Blockade.

REFERENCE: British Heart Journal, Vol. 29, pp., 671-683, 1967.

DRUGS: Propranolol (5 mg infused i.v. over a 5-min period)

SUBJECTS: 15 volunteer pilots

PROCEDURES: Propranolol effect on HR and BP responses during simulated flight (Link trainer).

FINDINGS:
Propranolol caused a heart rate reduction of 12 beats/min. During simulated flight, the rise was significantly smaller, 70 as compared to 96 beats/min before propranolol. The brachial arterial pressure measured at rest was unchanged after propranolol, and the response to simulated flight was similar to that before the administration of propranolol. Brachial arterial pulse was unaltered. Cardiac output at rest decreased and stroke volume decreased. The calculated peripheral resistance rose markedly. Simulated flight performance was unaffected by the drug.

INDEX: Propranolol, HR, BP, Complex Performance, Human.

300

AUTHORS: Fager, G., Beglund, G., Bondjers, G., Elmfeldt, D., Lager, I., Olofsson, S. O., Smith, U., and Wiklund. O.

TITLE: Effects of Anti-Hypertensive Therapy on Serum Lipoproteins Treatment with Metoprolol, Propranolol and Hydrochlorothiazide.

REFERENCE: Artery, Vol. 11, pp. 283-296, 1983.

DRUGS: Metoprolol (100 mg twice daily)
Propranolol (80 mg twice daily)
Hydrochlorothiazide (25 mg twice daily)

SUBJECTS: 31 men with untreated hypertension

PROCEDURES: Blood was obtained by venipuncture. Cholesterol and triglycerides were determined by enzymatic procedures. Apolipoproteins A-I, A-II, and B were measured in whole serum; insulin by radioimmunoassay; and glucose peroxidase method. Adrenalin, noradrenalin, and 4-hydroxy-3-methoxy-mandelate were determined from urinanalysis. Total adipose tissue lipoprotein lipase was measured using the Nilsson-Ehle procedure.

FINDINGS:
All three drugs increased serum triglyceride and VLDL-cholesterol levels. Propranolol produced consistent decreases in HDL-cholesterol, ApoA-I, and A-II levels. Propranolol produced an increase in adipose tissue lipoprotein lipase activity and a decrease in serum free fatty acids. No significant changes occurred in glucose tolerance or catecholamine excretion. The reduction in blood pressure was similar for all three drugs.

INDEX: Metoprolol, Propranolol, Hydrochlorothiazide, Biochemistry, BP, Human.

AUTHORS: Faulkner, S. L., Hopkins, J. T., Boerth, R. C., Young, J. L, Jellet, L. B., Nies, A. S., Bender, H. W., and Shand, D. G.

TITLE: Time Required for Complete Recovery from Propranolol.

REFERENCE: New England Journal of Medicine, Vol. 289, pp. 607-609, 1973.

DRUGS: Propranolol (40-240 mg/d in man and 20 mg/kg, i.p., in rats)

SUBJECTS: 8 bypass surgery patients and 6 male rats

PROCEDURES: Samples of plasma and left atrium were obtained during coronary bypass surgery from patients in which chronic propranolol treatment had been discontinued 24-72 h previously. Rats were killed at various times post-injection and tissue samples were analyzed.

FINDINGS:
Data confirmed previous reports that the half-life of propranolol in man was 3.4-6 h. In the rat, the half-life was approximately 1 h. There was no evidence of a long-lasting pool of the drug in the heart. No propranolol could be detected in the human plasma 48 h after injection.

INDEX: Propranolol, Biochemistry, Histology, Human, Nonhuman.

AUTHORS: Ferguson, D. W., Thames, M. D., and Mark, A. L.

TITLE: Effects of Propranolol on Reflex Vascular Responses to Orthostatic Stress in Humans (Role of Ventricular Baroreceptors).

REFERENCE: Circularion, Vol. 67, pp. 802-807, 1983.

DRUGS: Propranolol (0.1 mg/kg, i.v.)

SUBJECTS: 10 healthy male volunteers, ages 23-30

PROCEDURES: Forearm blood flow measured by occlusion plethysmography. Blood pressure measured by sphygmomanometry. Heart rate and rhythm were monitored continously using an ECG. Carotid baroreceptors were inhibited by applying neck pressure. Measured response to lower body negative pressure (LBNP) based on assumption that upright posture results in blood pooling in legs and therefore reduced pressure.

FINDINGS:
Propranolol reduced responses to LBNP at -40 mm Hg. In contrast, propranolol did not attentuate increases in forearm vascular resistance during the cold pressor or handgrip tests, thus excluding a nonspecific depression of reflexes. The drug had no significant effect on the vasoconstriction responses to neck pressure.

INDEX: Propranolol, HR, BP, Exercise, Stress, Human.

AUTHORS: Ferguson, R. K., Vlasses, P. H., Koffer, H., Clementi, R. A., Koplin, J. R., and Wilcox, C. M.

TITLE: Effect of Captopril and Propranolol, Alone and in Combination, on the Responses to Isometric and Dynamic Exercise in Normotensive and Hypertensive Men.

REFERENCE: Pharmacotherapy, Vol. 3, pp. 125-130, 1983.

DRUGS: Captopril (50 mg single oral administration)
Propranolol (80 mg single oral administration)

SUBJECTS: 5 aged-matched normotensive and 5 essential hypertensive men, ages 19-43

PROCEDURES: Isometric hand-grip exercise was performed using 50% maximum voluntary contraction for 2 min at 80 and 180 min following drug administration. Dynamic exercise was performed for 4 min on a Monark bicycle ergometer.

FINDINGS:
Captopril was indistinguishable from placebo after both isometric and ergometric exercise. Propranolol suppressed heart rate after both forms of exercise and tended to decrease systolic blood pressure only in the hypertensive groups; when combined with captopril, the results were not altered. The data imply that in sodium-replete subjects undergoing short-term vigorous exercise, the renin-angiotensin system, as measured by captopril inhibition, is less critical than the sympathoadrenal system, as measured by propranolol inhibition, in both normal and hypertensive men.

INDEX: Captopril, Propranolol, Exercise, HR, BP, Human.

AUTHORS: Fleminger, R.

TITLE: Visual Hallucinations and Illusions with Propranolol.

REFERENCE: British Medical Journal, Vol. 1, p. 1182, 1978.

DRUGS: Propranolol, Sotalol, Pindolol

SUBJECTS: 77 patients attending a hypertension clinic

PROCEDURES: Observations and case reports.

FINDINGS:
Eleven (17.5%) of these patients were found to have recurrent visual perception disorders. Visual hallucinations were recurrent in six of the patients and had occurred as isolated incidents in two patients who thought they were dreaming. Examples of recurrent visual hallucinations (furniture and clothes appearing to change into animals and people) occurred in 10 patients; distortions of spatial allocation and perspective also occurred with displacement of furniture or opening doors.

INDEX: Propranolol, Sotalol, Pindolol, Vision, Psychology, Human.

AUTHORS: Folgering, H., Rutten, H., and Roumen, Y.

TITLE: Beta-blockade in the Hyperventilation Syndrome. A Restrospective Assessment of Symptoms and Complaints.

REFERENCE: Respiration, Vol. 44, pp. 19-25, 1983.

DRUGS: Propranolol (30-80 mg)
Metoprolol (100-200 mg)
Tranquilizers (type not specified)

SUBJECTS: 73 patients suffering from hyperventilation syndrome

PROCEDURES: The following were measured: ventilation, respiratory frequency, arterial PCO_2, reaction to ventilation (increase or decrease) to increased arterial PCO_2, fast or slow recovery of arterial PCO_2 after 1 min voluntary hyperventilation, recognition of the complaints during this voluntary hyperventilation, and base excess.

FINDINGS:
Beta-blockade made the arterial PCO_2 increase, as did the tranquilizers. The change in subjective complaints were the same in all groups. Beta-blockade increased mean respiratory frequency as compared to the tranquilizers.

INDEX: Propranolol, Metoprolol, Tranquilizers, Ventilation, Human.

AUTHORS: Folgering, H. and Van Bussel, M.

TITLE: Maximal Exercise Power After a Single Dose of Metoprolol and of Slow-release Metoprolol.

REFERENCE: European Journal of Pharmacology, Vol. 18, pp. 225-229, 1980.

DRUGS: Metoprolol (300, 200, and 200 mg slow release, single dose)

SUBJECTS: 6 healthy male volunteers (medical students), ages 22-28

PROCEDURES: Exercise was performed on a Lode bicycle ergometer. Peak expiratory flow rate was measured using a Wright Peak Flowmeter. Blood pressure, heart rate, ECG, and blood gas values were measured. Single oral doses were used in a double-blind cross-over study.

FINDINGS:
Heart rate at rest was significantly lower after all doses of metoprolol. During max exercise, heart rate was considerably less with the drug. Systolic BP was lower at rest only after the 300 mg dose. Systolic BP during max exercise was markedly less for all dosages. Diastolic BP was not affected by dose or condition. Max exercise power was reduced in all but the 200 mg dosage. Twenty-four hours after the ingestion of the drug, there was no difference between the drug and placebo for the above mentioned variables; except that peak expiratory flow rate for metoprolol 200 mg was significantly lower as compared to placebo.

INDEX: Metoprolol, Exercise, Ventilation, BP, HR, Biochemistry, Human.

AUTHORS: Foster, C. A. and Aston, S. J.

TITLE: Propranolol-epinephrine Interaction: A Potential Disaster.

REFERENCE: Plastic and Reconstructive Surgery, Vol. 72, pp. 74-78, 1983.

DRUGS: Propranolol and several other drugs.

SUBJECTS: 5 females and 1 male, ages 52+

PROCEDURES: Six case studies.

FINDINGS:
Propranolol-epinephrine interaction is potentially fatal in certain sensitive indiviuals. The combined use of the two drugs can be characterized by a marked hypertensive episode followed by a reflex bradycardia. In such cases, the beta effect of epinephrine is blocked peripherally by propranolol and the alpha response leads to a paradoxical hypertension. The article presents a brief review of six case reports.

INDEX: Propranolol, Epinephrine, Pharmacology, Human.

AUTHORS: Froehling, S. D.

TITLE: Assessment of Behavioral and Physiological Functioning in Elderly Males.

REFERENCE: Dissertation Abstracts International, Vol. 35, p. 6070, 1975.

DRUGS: Propranolol

SUBJECTS: 12 elderly male volunteers

PROCEDURES: Subjects performed a paired-associate verbal learning task and a reaction time task on three successive days, with and without the drug. Physiological indices included heart rate, galvanic skin response (GSR), free fatty acids, and heart rate deceleration.

FINDINGS:
Results demonstrated that propranolol did have a significant effect in lowering heart rate. Levels of free fatty acids did not vary significantly. Measures of GSR did not show a difference across conditions. The hypothesis that a significant deceleration in heart rate would occur during the preparatory interval of the reaction time task was confirmed. The amplitude of the contingent negative variation was comparable to that found in young subjects in a similar experiment.

INDEX: Propranalol, Complex Performance, HR, Sweating, Biochemistry, Neuroelectric, Human.

390

AUTHORS: Furberg, C.

TITLE: Adrenergic Beta-blockade and Physical Working Capacity.

REFERENCE: Acta Medica Scandinavica, Vol. 182, pp. 119-127, 1967.

DRUGS: Propranolol (10-20 mg, depending on body weight)

SUBJECTS: Persons examined at the Dept. of Clinical Physiology over a period of 1.5 years (patients and nonpatient volunteers)

PROCEDURES: Subjects were divided into three groups: low, normal, or high physical working capacity at a pulse rate of 170 beats/min (W170). Physical working capacity, heart volume, and total hemoglobin were taken.

FINDINGS:
Patients with a low physical working capacity almost doubled their W170 after propranolol. In normal subjects, the effect was less, an increase of about 20%. In athletes the mean increase in W170 was less than 10%, and the maximal working capacity decreased slightly in most cases.

INDEX: Propranolol, Exercise, HR, Biochemistry, Human.

400

AUTHORS: Gershon, E. S., Goldstein, R. E., Moss, A. J., and Kammen, D. P.

TITLE: Psychosis with Ordinary Doses of Propranolol.

REFERENCE: Annals of Internal Medicine, Vol. 90, p. 938, 1979.

DRUGS: Propranolol (40 mg)

SUBJECTS: One 21-year-old woman (normal volunteer when admitted)

PROCEDURES: Initially given 14-d placebo treatment.

FINDINGS:
The patient showed no psychological changes in response to the placebo. Two days after beginning the propranolol, she started to become schizophrenic in her thoughts and behavior; this included intense hallucinations. The article discusses other cases where propranolol has been associated with abnormal mental states. The authors mention that propranolol is a potent antagonist of serotonin binding in vitro, which might account for the induced psychosis.

INDEX: Propranolol, Psychology, Human.

AUTHORS: Glaister, E. H.

TITLE: Effects of Beta Blockers on Psychomotor Performance-A Review.

REFERENCE: Aviation, Space, Environmental Medicine, Vol. 52, pp. 23-30, 1981.

DRUGS: Beta-blockers in general

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
By their specific peripheral action, beta-blockers must inevitably interfere with the body's adrenergic response to stress. Depression of this adrenergic response could be expected to improve certain aspects of psychomotor performance. Beta-blockers could have central action, and so modify performance directly. Since this effect must depend on penetration of the blood brain barrier, it would be expected that an agent with high lipid solubility (propranolol) would have more of a central effect than the more hydrophilic drugs (atenolol and sotalol). The author concludes that clinical usage of these agents may produce an adverse effect on flying, but that this would be no greater than changes seen on a day-to-day basis and probably less than those caused by many other "accepted" risks, i.e., alcohol. Furthermore, by selecting hydrophilic beta-blockers, risk should be reduced.

INDEX: Propanolol, Atenolol, Sotalol, Review, Complex Performance, Human.

AUTHORS: Grabowski, B. S., Cady, W. J., Young, W. W., and Emery, J. F.

TITLE: Effects of Acute Alcohol Administration on Propranolol Absorption.

REFERENCE: International Journal of Clinical Therapy and Toxicology, Vol. 18, pp. 317-319, 1980.

DRUGS: Propranolol (80 mg) crushed and dissolved in either saline or ethanol

SUBJECTS: 5 normal volunteers (4 males and 1 female), ages 19-31

PROCEDURES: Plasma concentrations were determined by high pressure liquid chromatography.

FINDINGS:
There was an increase in the area under the plasma concentration time curve and maximum plasma concentration when alcohol was administered with propranolol.

INDEX: Propranolol, Alcohol, Pharmacology, Human.

AUTHORS: Granville-Grossman, K. L., and Turner, P.

TITLE: The Effect of Propranolol on Anxiety.

REFERENCE: Lancet, Vol. 1, pp. 788-790, 1966.

DRUGS: Propranolol (20 mg)

SUBJECTS: Outpatients attending the Department of Psychological Medicine. All patients had symptoms associated with depression, organic brain disease, or schizophrenia; those with heart-disease or bronchial asthma were excluded.

PROCEDURES: Three types of assessment: (1) Investigator subjective evaluation, (2) investigator-rated anxiety on a 5-point scale, and (3) self-rated anxiety on a 5-point scale.

FINDINGS:
Findings indicated that propranolol in a dose of 20 mg, b.i.d., has a beneficial effect in anxiety. They suggested that this is principally due to alleviation of autonomically mediated symptoms, consistent with the findings that sinus tachycardia in anxious patients is abolished by i.v. administration of the drug. The improvement in the mental symptoms of the patients was not significant although there was an overall improvement judged by the investigator's ratings.

INDEX: Propranolol, Psychology, Human.

AUTHORS: Grimby, G. and Smith, U.

TITLE: Beta-Blockade and Muscle Function.

REFERENCE: Lancet, Vol. 2, p. 1318, 1978.

DRUGS: Propranolol (80 mg twice a day)
Metoprolol (100 mg twice a day)

SUBJECTS: 6 healthy volunteers (3 males and 3 females), ages 23-24

PROCEDURES: The subjects were given the above drugs or placebo for a 3-day period. Isometric and dynamic muscle strength was measured for the right quadriceps (Cybex II). Right handgrip strength was measured with a strain-gauge dynamometer.

FINDINGS:
Heart rate during exercise was significantly lowered by both drugs. Static muscle strength for the quadriceps and the handgrip and quadriceps dynamic strength at angular velocities between 30° and $180^{\circ}/s$ did not change with either drug. The reduction in torque after 50 repeated quadriceps contractions was 62.3 + 2.5, 59.7 + 3.2, and 58.7 + 3.9% for propranolol, metoprolol and placebo, respectively. The percentage reduction in handgrip force during the endurance test was 26.7 + 4.5., 26.7 + 5.0%, and 25.7 + 1.7% for the respective groups. The coordination test did not show a significant change with the beta-blockade.

INDEX: Propranolol, Metoprolol, Exercise, Human.

AUTHORS: Halleran, T. J.

TITLE: Propranolol and Eye Symptoms.

REFERENCE: Journal of the American Medical Association, Vol. 241, p. 2784, 1979.

DRUGS: Propranolol (80-160 mg/d)

SUBJECTS: One 70-year-old man with hypertension

PROCEDURES: Observations during three separate courses of propranolol therapy.

FINDINGS:
The patient had a sensation of dry gritty eyes and marked nocturnal photophobia. Several other drugs were being administered concurrently.

INDEX: Propranolol, Vision, Human.

AUTHORS: Harri, M.

TITLE: Beta-blockade and Physical Training in Rats.

REFERENCE: Annals of Clinical Research, Vol. 14, pp. 168-172, 1982.

DRUGS: Propranolol (10 mg/kg, s.c.)

SUBJECTS: Rats

PROCEDURES: Animals underwent physical training periods lasting 5 weeks (swimming and running). Each drug or non-drug test was performed at 24 h post-exercise. Biochemical analysis was performed on selected tissue samples.

FINDINGS:
Animals trained by swimming displayed several physiological changes: increased brown fat, hypertrophy of heart muscle, resting bradycardia, increased tachycardic and tail skin temperature response to isoprenaline, increased calorigenic response to noradrenaline, and slowed cooling in cold water. These changes were similar to those induced by cold acclimation or from repeated injections of noradrenaline. Propranolol administered with the training acted to reduce these changes.

INDEX: Propranolol, Exercise, Histology, Nonhuman.

AUTHORS: Hartley, L. R., Ungapen, S., Davie, I., and Spencer, D. J.

TITLE: The Effect of Beta-Adrenergic Blocking Drugs on Speaker's Performance and Memory.

REFERENCE: British Journal of Psychiatry, Vol. 142, pp. 512-517, 1983.

DRUGS: Propranolol (40 mg)

SUBJECTS: 16 volunteers (8 females and 8 males), ages 19-57

PROCEDURES: Subjects stood before a video camera and were given 1 min to prepare a 3-min talk on either anxiety-producing episodes in their lives or their feelings about giving electric shocks to human volunteers. Anxiety was assessed using the Spielberger State Anxiety Inventory.

FINDINGS:
Propanolol significantly reduced self-reported state anxiety scores. The mean state score was 52.5 following placebo treatment and 40.98 following propranolol treatment. Anxiety observed by the three raters was also significantly lower with propranolol. Following the placebo treatment, the mean anxiety score was 11.56, and following the propranolol, it was 9.54 on a 20-point scale. Additional results demonstrated that propranolol had no clear anxiolytic effect on autonomic function, since pulse rates were decreased equally in the anxious and non-anxious subjects, despite the higher initial pulse rate in the anxious group.

INDEX: Propranolol, Stress, Psychology, HR, Human.

AUTHORS: Hiatt, W. R., Demerick, F., Zerbe, G., Byyny, R., and Nies, A.

TITLE: Selective and Nonselective Beta-blockade of the Peripheral Circulation.

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 35, pp. 12-18, 1984.

DRUGS: Propranolol (80, 160, 240, and 320 mg/day)
Metoprolol (100, 200, 300, and 400 mg/day)

SUBJECTS: 10 healthy men, ages 20 to 30 years

PROCEDURES: The two drugs were compared using a randomized, double-blind, crossover design. Subjects were studied in the supine position with their feet on the pedals of a bicycle ergometer with the calf above the level of the heart. ECG was monitored continuously, and blood pressure was measured in the left arm using a cuff. Subjects exercised at three work loads: 300, 600, and 900 kg meter/min.

FINDINGS:
Metoprolol lowered resting and exercise mean blood pressure at most doses; propranolol had less effect. Neither drug altered resting or exercise calf blood flow or vascular resistance. In normal subjects, metoprolol was more effective in lowering blood pressure during exercise.

INDEX: Propranolol, Metoprolol, Exercise, BP, HR, Human.

AUTHORS: Hinshelwood, R. D.

TITLE: Hallucinations and Propranolol (Correspondence).

REFERENCE: British Medical Journal, Vol. 1, p. 766, 1969.

DRUGS: Propranolol (40 mg, q.i.d.)

SUBJECTS: One 53-year-old man

PROCEDURES: Case report.

FINDINGS:
The man suffered from nighttime hallucinations. He described spirits that appeared in his bedroom and stood still, worked spells, or copulated. This commenced when the patient first began taking propranolol (4-5 months ago). He also described tactile hallucinations "like little darts dropped on the skin." When propranolol treatment was discontinued, the hallucinations also stopped. One month later, the propranolol was restarted, and the hallucinations did not recur. The patient had no previous history of mental disturbance, epilepsy or drug or alcohol abuse.

INDEX: Propranolol, Psychology, Human.

AUTHORS: Hirshman, C. A. and Downes, H.

TITLE: A Possible Undesirable Action of Propranolol and Atropine.

REFERENCE: Anesthesiology, Vol. 53, p. 521, 1980.

DRUGS: Propranolol (2 mg/kg)
Atropine (0.4 mg/kg)

SUBJECTS: Thiamylal-anesthetized dogs

PROCEDURES: The drugs were administered in combination during surgery.

FINDINGS:
Emergence delirium in these dogs consisted of prolonged running movements while in the lateral decubitus position, repetitive loud whining, fixed stare, and complete lack of contact with surroundings. Within 5 min of receiving physostigmine (1-2 mg, i.v.), the animals became responsive, assumed an upright position, and walked around their cages. This effect did not occur with either drug alone.

INDEX: Propranolol, Atropine, Nonhuman.

AUTHORS: Horn, J., Rylander, M. L., and Hicks, H. M.

TITLE: Propranolol-induced Hallucinosis.

REFERENCE: Clinical Pharmacology, Vol. 1, pp. 464-468, 1982.

DRUGS: Propranolol

SUBJECTS: 18 case reports, various ages

PROCEDURES: Case reports.

FINDINGS
Eighteen persons who suffered hallucinations after using propranolol. Case descriptions.

INDEX: Propranolol, Psychology, Human.

AUTHORS: Houben, H.

TITLE: Hemodynamic Effects of Isometric Exercise and Mental Arithmetic in Hypertension Treated with Selective and Nonselective Beta-blockade.

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 34, pp. 164-169, 1983.

DRUGS: Propranolol (240 mg/day)
Metoprolol (300 mg/day)

SUBJECTS: 25 patients being treated for hypertension

PROCEDURES: Double-blind crossover design. Experiments with isometric exercise and with mental arithmetic were performed in one session at the end of each 4-week treatment. Blood pressure, heart rate, and forearm blood flow were measured three times. Plasma levels were checked by gas chromatography.

FINDINGS:
Both drugs reduced basal blood pressure as well as heart rate. Both medications had equal effect on lowering blood pressure during exercise (handgrip) or mental arithmetic.

INDEX: Propranolol, Metoprolol, Exercise, Complex Performance, BP, HR, Biochemistry, Human.

AUTHORS: Hughson, R. L. and McFarlane, B. J.

TITLE: Effect of Oral Propranolol on the Anaerobic Threshold and Maximum Exercise Performance in Normal Man.

REFERENCE: Canadian Journal of Pharmacology, Vol. 59, pp. 567-573, 1981.

DRUGS: Propanolol (160 mg/day)

SUBJECTS: 6 healthy males, ages 19-21

PROCEDURES: Subjects performed a progressive cycle ergometer test to a fatigue-limited maximum with and without the drug. Respiratory gas exchange was monitored continuously. The anaerobic threshold was determined by a point of departure from a linear relationship between ventilation and oxygen uptake and by the rise of blood lactate concentrations.

FINDINGS:
Propranolol produced a significant reduction in heart rate at all power outputs (20-45 bpm). During light and moderate exercise, there was no significant difference in oxygen uptake, ventilation, or blood lactate. There was no difference in anaerobic threshold; however, propranolol did significantly reduce heart rate at the anaerobic threshold. Above the aerobic threshold, there was no significant difference of oxygen uptake at any power output level.

INDEX: Propranolol, Exercise, HR, Ventilation, Biochemistry, Human.

AUTHORS: Hughson, R. L. and Smyth, G. A.

TITLE: Slower Adaptation of Vo_2 to Steady State of Submaximal Exercise with Beta-blockade.

REFERENCE: European Journal of Applied Physiology, Vol. 52, pp. 107-110, 1983.

DRUGS: Propranolol (40 mg) and Metoprolol (50 mg)

SUBJECTS: 17 normal subjects

PROCEDURES: The study assessed the effects of beta-blockade on the kinetics of oxygen uptake (VO_2). Beta-Blockade was achieved using either metoprolol (50 mg, p.o.) or propranolol (40 mg, p.o.); each drug was administered twice a day. The cycle ergometer was used to assess work rates at approximately 80% of the ventilatory anaerobic threshold at 2 d, 1 week, and 4 weeks post-drug administration.

FINDINGS:
Beta-blockade adaptation did not affect the plateau values for VO_2. The drugs reduced the rate of adaption to steady state. This effect produced an increase in the oxygen debt and a reduction in CO_2 rebreathing. Blood lactate levels were not affected by either drug.

INDEX: Propranolol, Metoprolol, Exercise, Ventilation, Biochemistry, Human.

AUTHORS: Hull, D. H.

TITLE: Mild Hypertension.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 56, pp. 304-309, 1985.

DRUGS: Various beta-blockers including Propranolol

SUBJECTS: NA

PROCEDURES: A review of beta-blockers.

FINDINGS:
The article briefly reviews the antihypertensive drug treatments and summarizes the results of some therapeutic trials. "Despite the success of drug treatment, any effect on the occurrence of coronary events or of coronary deaths is slight. Reasons for this disappointing outcome are suggested, and the implications for the treatment of hypertensive aviators are explored."

INDEX: Propranolol, Atenolol, Nadolol, Pindolol, Metoprolol, Review, Human.

AUTHORS: Hutchinson, P. F. and Harrison, R. N.

TITLE: Effect of Acute and Chronic Beta-blockade on Carbon Dioxide Sensitivity in Normal Man.

REFERENCE: Thorax, Vol. 35, pp. 869-872, 1980.

DRUGS: Propranolol, Atenolol, and Metoprolol

SUBJECTS: 8 adults (6 males and 2 females)

PROCEDURES: A modified Read rebreathing method was used to produce a progressive hypercapnia. CO_2 was assessed by an infrared analyzer. Ventilation was measured by displacement of air from a bag-in-box arrangement. Mouth pressure was measured using a pressure transducer. A series of exercise tests (4 min each) were carried out on an electronically braked cycle ergometer. Heart rate was measured by ECG.

FINDINGS:
None of the above drugs produced any serious side effects. All subjects were able to sense an increase in muscle fatigue from the drugs during the exercise tests. No significant change was reported in either the slope or x-intercept of ventilation for any of the treatments. The results indicated a highly significant reduction in exercise tachycardia. None of the drugs produced a significant alteration in carbon dioxide sensitivity. The forced expiratory volume for 1 s was unaltered by any of the drugs.

INDEX: Propranolol, Atenolol, Metoprolol, Ventilation, Exercise, HR, Human.

570

AUTHORS: Jauchem, J. R., Frei, M. R., and Heinmets, F.

TITLE: Increased Susceptibility to Radiofrequency Radiation Due to Pharmacological Agents.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 55, pp. 1036-1040, 1984.

DRUGS: Propranolol, Chlorpromazine, and Methysergide

SUBJECTS: Rats

PROCEDURES: Colonic temperature was monitored continuously with a Vitek 101 temperature probe. ECG was recorded using a special method. The left carotid artery was catheterized for measurement of blood pressure. Post-surgery, the animal was positioned in a Plexiglas holder for exposure to RF. The RF fields were generated by a type 1326 generator and sent by a Model 110S antenna.

FINDINGS:
Propranolol, chlorpromazine and methysergide all acted to reduce survival time. The propranolol treated animal survived the shortest time and had the lowest tolerance to increased temperature. During terminal exposure to RFR, although the heart rate continued to increase (temperatures above 41C, colonic), blood pressure tended to decrease. Chlorpromazine decreased survival time 31%. Methysergide decreased survival time (27%). Propranolol decreased the survival time by 42%.

INDEX: Propranolol, Chlorpromazine, Methysergide, Heat Stress, HR, BP, Nonhuman.

580

AUTHORS: Jezova, D., Vigas, M., Klimes, I., and Jurcovicova, J.

TITLE: Adenopituitary Hormone Response to Exercise Combined with Pr pranolol Infusion in Man.

REFERENCE: Endocrinologia Experimentalis, Vol. 17, pp. 91-98, 1983.

DRUGS: Propranolol (two infusion rates, 0.32 mg/min and 0.08 mg/min, for a total of 5.36 mg)

SUBJECTS: 12 healthy male untrained volunteers, ages 20-23

PROCEDURES: Subjects were pretreated, then exercised; later blood and urine samples were taken.

FINDINGS:
Propranolol (i.v.) resulted in an increase in plasma growth hormone to exercise. Propranolol potentiated the response of plasma cortisol level to submaximal exercise. There was no change in urinary free cortisol or 17-OHCS during exercise. The increase of serum prolactin with exercise was unaffected by propranolol.

INDEX: Propranolol, Exercise, Biochemistry, Human.

590

AUTHORS: Joseph, N. T., Gupta, A. D., and Gupta, J. S.

TITLE: Effect of Propranolol on Work Capacity at Simulated High Altitude.

REFERENCE: Indian Journal of Physiology and Pharmacology, Vol. 16, pp. 219-225, 1972.

DRUGS: Propranolol (120 mg/day)

SUBJECTS: 11 soldiers

PROCEDURES: Three sets of observations were made: (a) at ambient pressure of Delhi; (b) at a pressure of 750mm Hg in a low pressure chamber; and (c) at 480mm Hg in the low-pressure chamber. Resting heart rate, resting lactate level, max O_2 uptake capacity, max exercise ventilation, max heart rate, and max blood lactate were all measured.

FINDINGS:
Propranolol did not affect the work capacity for prolonged physical effort as judged by the measurement of maximum oxygen uptake capacity. The drug caused a significant reduction in the resting heart rate, but the maximum heart rate attained at maximum work rate was not significantly different.

INDEX: Propranolol, HR, BP, Biochemistry, Ventilation, Exercise, Human.

600

AUTHORS: Joseph, V. P., Badrinath, K., Adithan, C., Shetty, P. S., and Joseph, T.

TITLE: Effect of Propranolol on Task Performance in Human Volunteers.

REFERENCE: Indian Journal of Medical Research, Vol. 77, pp. 384-387, 1983.

DRUGS: Propranolol (40 mg)

SUBJECTS: 10 normal healthy medical students, ages 17-19

PROCEDURES: A double-blind study on task performance in competitive and non-competitive situations. Reaction time to randomly chosen colors and steadiness of hand were measured.

FINDINGS:
Propranolol significantly reduced the reaction time and produced a steadying effect in the competitive situation.

INDEX: Propranolol, Complex Performance, Stress, Human.

610

AUTHORS: Kaijser, L., Kaiser, P., Karlsson, J., and Rossner, S.

TITLE: Beta-blockers and Running.

REFERENCE: American Heart Journal, Vol. 100, p. 943, 1980.

DRUGS: Propranolol (80 mg)
Atenolol (100 mg)

SUBJECTS: Healthy volunteers (N not given)

PROCEDURES: Subjects ran a 2000 m course with and without beta-blockers.

FINDINGS:
Individuals with a high concentration of slow twitch fibers took 20 to 30% longer to run the course while under the influence of propranolol. On atenolol, the same individuals needed less than 10% more time to complete the course.

INDEX: Propranolol, Atenolol, Exercise, Human.

620

AUTHORS: Kalischer, A. L., Johnson, L. L., Johnson, Y. E., Stone, J., Feder, J. L., Escala, E., and Cannon, P. J.

TITLE: Effects of Propranolol and Timolol on Left Ventricular Volumes During Exercise in Patients with Coronary Disease.

REFERENCE: Journal of the American College of Cardiology, Vol. 3, pp. 210-218, 1984.

DRUGS: Propranolol (240 mg)
Timolol (60 mg)

SUBJECTS: 18 patients with coronary disease

PROCEDURES: Radionuclide angiogram at rest and exercise. Pulse and blood pressure checked. The left ventricular border and the intensity and spatial distribution of background isotope counts were defined by computer analysis. A representitive cardiac cycle was constructed from end-diastolic and end-systolic beats.

FINDINGS:
The ejection fraction at rest after beta-receptor blockade was not significantly different from pretreatment measurements because of an increase in both end-diastolic and end-systolic volumes. The value for peak systolic pressure/end-systolic volume index at rest was lower after treatment. With exercise, the ejection fraction increased and was greater after treatment, owing to an increased end-diastolic volume and unchanged end-systolic volume. The left ventricular functional response to exercise did not normalize with therapy. Comparisons of regional functional changes during exercise before and after treatment showed improvement or no change in ischemic segments. The data imply that beta-blockade improves global ventricular function slightly by reversing the ischemic response, but, it blunts the inotropic responses of the normal exercise heart muscle to sympathetic stimulation.

INDEX: Propranolol, Timolol, Exercise, HR, BP, Biochemistry, Human.

630

AUTHORS: King, W. H., Lancaster, M. C., and Cloyd, D. E.

TITLE: Antihypertensive Drug Therapy in USAF Flying Personnel.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 46, pp. 436-440, 1975.

DRUGS: NA

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
The reviewed data concerns hypertensive USAF aircrew members, as avaiable from the WAVR File (July 1973) and the records of the Aeromedical Consultation Service at USAFSAM (1 July 1972-30 June 1973). Of over 6500 entries in the WAVR File, hypertension was listed as a diagnosis for 754 individuals. Drug therapy had been instituted in 379 cases (50.3%). Statistics regarding rank, age, and aeronautical rating were presented. The group included 520 pilots, of whom 268 were receiving drug therapy. Associated medical conditions (e.g., abnormal EKG findings, carbohydrate intolerance, and hyperuricemia) are presented. Similar data are reviewed for the 84 patients evaluated on the Aeromedical Consultation Service (USAFSAM).

INDEX: Review, Human.

640

AUTHORS: Korol, B. and Brown, M. L.

TITLE: The Role of The Beta-adrenergic System in Behavior: Antidepressant Effects of Propranolol.

REFERENCE: Current Therapeutic Research, Vol. 9, pp. 269-279, 1967.

DRUGS: Propranolol (0.3, 1.0, and 3.0 mg/kg, i.v.)

SUBJECTS: Dogs

PROCEDURES: One dose per dog per week, each dog received all three doses. Ditran Rating Scale (DRS) scores were made at 15, 30, 60, 90 and 120 min. A second design measured the acute effects in conscious dogs of the test drug upon four physiological parameters: (1) systolic and diastolic arterial pressure; (2) heart rate; (3) respiration; and (4) rectal temperature.

FINDINGS:
With 0.3 mg/kg, propranolol was devoid of apparent effects on systolic and diastolic arterial pressures, heart rate, rectal temperature, and respiratory rate in conscious, loosely restrained dogs. With 3.0 mg/kg, propranolol produced a mild transient decrease in systolic and diastolic pressures and some associated tachycardia. Rectal temperature and respiration were not altered. Propranolol produced a dose-related reversal of the aberrant behavioral state in conscious dogs.

INDEX: Propranolol, BP, HR, Ventilation, Heat-stress, Nonhuman.

650

AUTHORS: Krantz, D. S., Durel, L. A., Davia, J. E., Shaffer, R. T., Arabian, J. M., Demdroski, T. M., and MacDougall, J. M.

TITLE: Propranolol Medication Among Coronary Patients: Relationship to Type A Behavior and Cardiovascular Response.

REFERENCE: Journal of Human Stress, Vol. 8, pp. 4-12, 1982.

DRUGS: Propranolol

SUBJECTS: 88 cardiac patients

PROCEDURES: Each subject was interviewed. The interviews were recorded, and later audited by two raters. Among the 88 patients, 16 were extreme type As, 52 mild type As, 13 were indeterminable, and 7 were classed as type B. During the interview and quiz, blood pressure and EKG were monitored. At the time of this testing 65 of the patients were medicated with propranolol and 23 were not medicated.

FINDINGS:
Results indicated that beta-blockers reduce the intensity of type A behavior as measured in structured interviews. Reactivity of heart rate and blood pressure were significantly attenuated in those patients taking propranolol.

INDEX: Propranolol, Stress, Psychology, HR, BP, Human.

660

AUTHORS: Krupin, T., Singer, P. R., Perlmutter, J., Kolker, A. E., and Becker, B.

TITLE: One-hour Intraocular Pressure Response to Timolol.

REFERENCE: Archives of Ophthalmology, Vol. 99, pp. 840-841, 1981.

DRUGS: 0.25% Timolol Maleate (1 drop topical)

SUBJECTS: 25 healthy, nontreated, ocular hypertensive patients

PROCEDURES: Baseline intra-ocular pressures (IOP's) were measured. Patients received one drop in one eye and IOP measured 1 h later. IOP remeasured 3-4 weeks later with treatment twice daily. Drug concentration was increased to 0.5% and measured again 3-4 weeks later.

FINDINGS:
Initial administration of Timolol reduced mean baseline pressure of 28.1mm Hg to 18.5 mm Hg. After 3-4 weeks of twice a day drug administration, mean IOP increased to 21.1 mm Hg. Reducing the drug concentration to 0.5% for 3-4 weeks did not produce a significant lowering of IOP.

INDEX: Timolol, Vision, Human.

AUTHORS: Lader, M. H. and Tyrer, P. J.

TITLE: Central and Peripheral Effects of Propranolol and Sotalol in Normal Human Subjects.

REFERENCE: British Journal of Pharmacology, Vol. 45, pp. 557-566, 1972.

DRUGS: Propranolol (120 mg)
Sotalol (240 mg)

SUBJECTS: 6 subjects (3 females and 3 males), ages 19-29)

PROCEDURES: Subjective self-rating scales to assess mood and body symptoms. An electroencephalogram was recorded. Finger tremor, skin conductance, auditory reaction time, and key tapping time were measured. Radial pulse was taken. Card-sorting, digit symbol substitution, and symbol copying tests were used.

FINDINGS:
No significant cognitive effects were reported with either drug. Sotalol did produce some drowsiness/muzziness, and both drugs caused subjects to feel somewhat 'troubled.' There was a significant drop in pulse rate for both drugs. No drug effects were shown with the tremor or skin conductance tests.

INDEX: Propranolol, Sotalol, Psychology, Neuroelectric, Musculoskeletal, HR, Auditory, Complex Performance, Human.

AUTHORS: Landauder, A. A., Jellett, L. B., and Kirk, J.

TITLE: Propranolol and Skilled Human Performance.

REFERENCE: Pharmacology, Biochemistry and Behavior, Vol. 4, pp. 283-287, 1976.

DRUGS: Propranolol (six doses at 40 mg/dose)

SUBJECTS: 18 male undergraduate students, ages 18-31

PROCEDURES: Tests included Profile of Mood States Questionaire, blood pressure and heart rate, Letter Substitution Test, Kinetic Visual Acuity Test, Serial Reaction Time Test, Dot Tracking Task, Steadiness Test, Martin Driving Simulator, and Choice Reaction Time Apparatus.

FINDINGS:
The Profile of Mood States Questionaire did not show a significant drug effect. The drug significantly reduced systolic blood pressure and heart rate. Of the motor and cognitive skill tests, only an increase in the variance of the response time on the Choice Reaction Time test was noted.

INDEX: Propranolol, Questionnaire, Psychology, BP, HR, Complex Performance, Vision, Musculoskeletal, Human.

690

AUTHORS: Langer, A. W., McCubbin, J. A. Stoney, C. M., Hutcheson, J. S., Charlton, J. D., and Obrist, P. A.

TITLE: Cardiopulmonary Adjustments During Exercise and an Adversive Reaction Time Task: Effects of Beta-adrenoceptor Blockade.

REFERENCE: Psychophysiology, Vol. 22, pp. 59-68, 1985.

DRUGS: Propranolol

SUBJECTS: 34 healthy, non-smoking males

PROCEDURES: This study was designed to compare cardiopulmonary and hemodynamic changes to bicycle exercise and a behavioral stressor (aversive reaction time). The purpose was to assess how beta-blockade mediated different types of physiological stressors. Measured factors included O_2 consumption, CO_2 production, pulmonary ventilation, end-tidal O_2 and CO_2, and heart rate. Fourteen subjects were pretreated with propranolol (4 mg, i.v.).

FINDINGS:
Propranolol reduced tachycardia induced by exercise but entirely abolished tachycardia induced by behavioral stress. No significant changes were reported in VO_2 or VCO_2 from rest for the beta-blocker group. It was concluded that the unwarranted increase in heart rate during adversive behavior testing is probably mediated by increased beta-adrenergic drive on the myocardium.

INDEX: Propranolol, Exercise, HR, BP, Ventilation, Stress, Human.

700

AUTHORS: Laverty, R. and Taylor, K. M.

TITLE: Propranolol Uptake into the Central Nervous System and the Effect on Rat Behavior and Amine Metabolism.

REFERENCE: Journal of Pharmacy and Pharmacology, Vol. 20, pp. 605-609, 1968.

DRUGS: Propranolol (administered i.p. and in the drinking water)

SUBJECTS: Rats

PROCEDURES: Brain assays for biogenic amines and metabolites.

FINDINGS:
After chronic oral administration, brain levels of propranolol were equal to those at 3 h post i.p. injection. Propranolol produced no significant change in central levels of norepinephrine, normetanephrine, dopamine, 3-methoxytyramine homovanillic acid, serotonin, or total indoles; nor did it cause changes in behavior.

INDEX: Propranolol, Histology, Nonhuman.

710

AUTHORS: Leenen, F. H., Boer, P., and Dorhout Mees, E. J.

TITLE: Antihypertensive Effect of Propranolol at Rest and During Exercise.

REFERENCE: British Journal of Clinical Pharmacology, Vol. 15, pp. 361-365, 1983.

DRUGS: Propranolol

SUBJECTS: 8 normal subjects

PROCEDURES: Over a 2-week period, subjects were given increasing doses of propranolol (80, 160, 320 mg/day and in three patients, 640 mg/day). According to the renin-sodium index, patients were classified as having normal-renin hypertension. The study conducted evaluations at rest and during exercise on a bicycle (Lode-ergometer) at a pedal frequency of 60 rev/min for 3 periods of 6 min each. Blood plasma was taken for drug assay.

FINDINGS:
Propranolol (80 mg/day) produced a marked decrease in the systolic blood pressure (11 + 4 mm Hg). At 160 mg/day a systolic BP drop of 16 + 4 mm Hg was measured. Diastolic BP reductions were 9 + 3 mm Hg and 12 + 3 mm Hg, respectively. Angiotensin I and the rise of systolic blood pressure, during bicycle exercise, were surpressed to a similar extent. At 80 mg daily, exercise tachycardia was reduced by 18%, at 160 mg by 28%, and at the 2 higher doses by 32%.

INDEX: Propranolol, Exercise, Biochemistry, BP, HR, Human.

720

AUTHORS: LeWinter, M. W., Crawford, M. H., Karliner, J. S., and O'Rourke, R. A.

TITLE: Effects of Oral Propranolol in Normal Subjects.

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 17, pp. 709-712, 1975.

DRUGS: Propranolol

SUBJECTS: 10 normal volunteers

PROCEDURES: The study was conducted over three sequential 2-week periods. The subjects received a placebo during the first 2-week period. During the second 2-week period, the subjects received the propranolol (40 mg every 6 h and 40 mg at bedtime). The subjects received the placebo for the last 2-week period. Several factors were investigated: (1) unusual symptoms, (2) resting heart rate and arterial pressure, (3) roentgenographic left heart dimension, (4) systolic time intervals, and (5) maximum treadmill exercise test was performed. Serum assays were conducted.

FINDINGS:
Mean serum level was 28 ng/ml. Supine resting heart rate dropped from 68 bpm to 56 bpm. Mean systolic BP also reduced from 125 to 114 mm Hg. Mean diastolic pressure did not change significantly. The average left ventricular ejection time index, the pre-ejection period index, and the ratio of the two were not significantly altered by the drug. A small decrease in exercise tolerance was reported. Mean left heart dimension was significantly changed. No adverse reactions to the drug were reported.

INDEX: Propranolol, HR, BP, Biochemistry, Exercise, Human.

AUTHORS: Light, K. E., Dick, T. E., and Hughes, M. J.

TITLE: Central and Peripheral Receptors in Guinea-pigs Exposed to Simulated High Altitude.

REFERENCE: Neuropharmacology, Vol. 23, pp. 189-195, 1984.

DRUGS: Radioactive Ligand Propranolol (10^{-5} Molar)
Radioactive Ligand Triprolidine (10^{-5} Molar)

SUBJECTS: Male guinea-pigs

PROCEDURES: The animals were exposed to a simulated high altitude of 6000 m (350 torr) in low-pressure chambers. Homogenate receptor studies were carried-out post-mortem.

FINDINGS:
Animals, chronically exposed (9 w) to high altitude, showed changes in some neurotransmitter-receptor systems. Cardiac beta-adrenergic receptor density decreased while receptor affinity increased. The levels of cardiac norepinephrine (NE) remained unchanged. Histamine receptor levels in the brain remained unchanged. Central DA receptor concentration remained unchanged. Thus, the major finding of this publication may be that chronic exposure to high altitude could possibly reduce the beta-adrenergic cardiac receptors in number but make them more responsive to NE or possibly the blockade of propranolol.

INDEX: Propranolol, Triprolidine, Histology, Stress, HR, Nonhuman.

AUTHORS: Lima, D. R. and Turner, P.

TITLE: Propranolol Increases Reduced Beta-receptor Function in Severely Anxious Patients.

REFERENCE: Lancet, Vol. 2, p. 1505, 1983.

DRUGS: Propranolol

SUBJECTS: 14 patients (8 males and 6 females)

PROCEDURES: Lymphocyte cyclic AMP analyses. cAMP responsiveness to isoprenaline as an anxiety indicator.

FINDINGS:
There appeared to be a significant difference in beta-adrenoceptor function between anxious patients and controls, similar to that found in hypertensive patients, which may represent a down-regulation. Treatment with propranolol but not diazepam resulted in an increased responsiveness similar to that found in hypertensive patients treated with beta-blockers.

INDEX: Propranolol, Biochemistry, Human.

AUTHORS: Lindenschmidt, R., Brown, D., Cerimele, B., Walle, T., and Forney, R. B.

TITLE: Combined Effects of Propranolol and Ethanol on Human Psychomotor Performance.

REFERENCE: Toxicology and Applied Pharmacology, Vol. 67, pp. 117-121, 1983.

DRUGS: Propranolol (160 mg in divided doses)
Ethanol (50 ml)

SUBJECTS: 12 male volunteers were selected from a group of medical and graduate students, ages 22-28, and weight 145-195 lbs

PROCEDURES: Test Battery: Modified Cornell Medical Index, Stability of Stance, Motor Performance, Manual Dexterity, Time Estimation, and Mental Performance (auditory feedback). Heart rate and blood pressure were monitored.

FINDINGS:
Propranolol antagonized the decrement in psychomotor performance produced by alcholol on The Pursuit Meter. In all the other tests, there was no significant drug effect. Propranolol alone had no significant effect on any of the tests.

INDEX: Propranolol, Alcohol, Complex Performance, HR, BP, Musculoskeletal, Human.

AUTHORS: Lund-Johansen, P.

TITLE: Long-term Hemodynamic Effects of Bunitrolol at Rest and During Exercise in Essential Hypertension.

REFERENCE: Journal of Cardiovascular Pharmacology, Vol. 1, pp. 77-83, 1979.

DRUGS: Bunitrolol (10-60 mg/day)

SUBJECTS: 11 men with untreated essential hypertension

PROCEDURES: The subjects were studied hemodynamically during strictly standardized conditions: at rest, supine, sitting, and during bicycling in steady state at 300, 600, and 900 kpm/min. Oxygen consumption was measured, as well as intra-arterial pressure and heart rate.

FINDINGS:
Sitting blood pressure dropped in all subjects, and mean heart rate decreased from 79 to 64 beats/min. Oxygen consumption did not change significantly. The cardiac index during supine rest decreased on average by 18% in all but two subjects. The mean cardiac index decrease was 23% at rest and 25% during exercise. The heart rate decreased in all but one subject during supine rest and in all subjects during sitting rest and exercise. During supine rest, there was no consistent change in the stroke index. At sitting rest, the stroke index decreased 9%. There was also a decrease in stroke index during exercise. Blood pressure was reduced in all subjects both at rest and during all work levels. At rest, supine and sitting there were no significant changes in total peripheral resistance. Total peripheral resistance was greater during exercise than pretreatment levels.

INDEX: Bunitrolol, Exercise, HR, BP, Ventilation, Human.

AUTHORS: Lundborg, P., Astrom, H., Bengtsson, C., Fellenius, E., Von Schenck, H., Svensson, L., and Smith, U.

TITLE: Effect of Beta-adrenoreceptor Blockade on Exercise Performance and Metabolism.

REFERENCE: Clinical Science, Vol. 61, pp. 299-305, 1981.

DRUGS: Propranolol (80 mg, b.i.d.)
Metoprolol (100 mg, b.i.d.)

SUBJECTS: 6 healthy male volunteers

PROCEDURES: Measured variables included heart rate (ECG); duration of exercise (bicycle ergometer); blood glucose; non-esterified fatty acids and glycerol levels; lactate, alanine, and potassium levels; glucagon; adrenaline; and noradrenaline.

FINDINGS:
Both drugs reduced the capacity to perform exercise. Blood glucose levels decreased during exercise with beta-blockade. At exhaustion, the average non-esterified fatty acid level had increased 256% on placebo, 148% after metoprolol, and 65% after propranolol. It was therefore concluded that the use of beta-blockers reduce the ability to do prolonged submaximal exercise by reducing the availability of substrates to the working muscles.

INDEX: Propranolol, Biochemistry, Exercise, HR, Human.

AUTHORS: MacDonald, H. R., Sapru, R. P., Taylor, S. H., and Donald, K. W.

TITLE: Effect of Intravenous Propranolol on the Systemic Circulatory Response to Sustained Handgrip.

REFERENCE: American Journal of Cardiology, Vol. 18, pp. 333-344, 1966.

DRUGS: Propranolol

SUBJECTS: 7 males, ages 30-51, none had any clinical evidence of heart disease

PROCEDURES: Handgrip was performed on a strain guage dynamometer (30% max voluntary contraction). Electrocardiogram and aortic blood pressure were recorded continuously. Cardiac output was determined at 2-min intervals.

FINDINGS:
A similar increase in the mean aortic pressure was seen before and after administration of the drug, but the cardiac output response was reduced and compensated by increased systemic vascular resistance. The percentage increase in heart rate during grip was greater after propranolol.

INDEX: Propranolol, Exercise, HR, BP, Human, Handgrip.

790

AUTHORS: Maksud, M. G., Tristani, F. E., Coutts, K. D., Barboriak, J. J., and Hamilton, L. H.

TITLE: Effects of Propranolol on Several Physiological Responses During Orthostatic and Exercise Stress in Healthy Males.

REFERENCE: Canadian Journal of Physiology and Pharmacology, Vol. 49, pp. 867-872, 1971.

DRUGS: Propranolol

SUBJECTS: 16 healthy young males

PROCEDURES: Resting heart rate, minute ventilation, and oxygen uptake were measured. Following drug administration, a standard tilt test was conducted. Heart rate and blood pressure were monitored. Plasma free fatty acids were measured before and after drug administration. A multistage exercise protocol was conducted following the tilt test.

FINDINGS:
Propranolol significantly lowered heart rate response to orthostatic stress, while both systolic and diastolic blood pressure measurements were unaffected. The drug reduced both heart rate and minute ventilation during exercise. Oxygen consumption and mean exercise endurance were not significantly affected. The results indicate that in healthy subjects the cardiac depressant effects of the drug are compensated, so that work capacity and oxygen uptake are not significantly reduced.

INDEX: Propranolol, HR, BP, Ventilation, Exercise, Human.

800

AUTHORS: Mishriki, A. A. and Weidler, D. J.

TITLE: Long-acting Propranolol (Inderal LA): Pharmacokinetics Pharmacodynamics and Therapeutic Use.

REFERENCE: Pharmacotherapy, Vol. 3, pp. 334-341, 1983.

DRUGS: Propranolol

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
The article follows the following outline: basic background information on propranolol; description of new long-acting formulation; pharmacokinetics and pharmacodynamics; effect of chronic dosing; therapeutic use (angina pectoris, hypertension, and hyperthyroidism); conclusions; and commentaries by other physicians and researchers.

INDEX: Propranolol, Review, Human.

AUTHORS: Mostyn, R. H. L.

TITLE: Tinnitus and Propranolol.

REFERENCE: British Medical Journal, Vol. 1, p. 776, 1969.

DRUGS: Propranolol (two 10-mg doses for 4 d then 10 mg daily for several weeks)

SUBJECTS: One 56-year-old woman

PROCEDURES: Case report.

FINDINGS:
The woman was started on propranolol for mild hypertension. Within a few hours, she noticed ringing in her ears. She took only ten-mg twice daily for 4 days then reduced the dose to once a day, which stopped the ringing in the ears. A few weeks later when the dose was restored to twice daily, she developed tinnitus. The patient found the effect too unpleasant for treatment to continue.

INDEX: Propranolol, Human.

AUTHORS: Mustchin, C. P., Gribbin, H. R., Tattersfield, A. E., and George, C. F.

TITLE: Reduced Respiratory Responses to Carbon Dioxide After Propranolol: A Central Action?

REFERENCE: British Medical Journal, Vol. 2, pp. 1229-1231, 1976.

DRUGS: Propranolol (80 mg)

SUBJECTS: 6 healthy volunteers, ages 22-35

PROCEDURES: Progressive hypercapnia was produced by rebreathing a mixture of 5% CO_2 in oxygen. Ventilation was determined by displacing air from a bag in bottle arrangement. Spirometry was performed before and after drug administration.

FINDINGS:
Propranolol significantly reduced CO_2 responsiveness and eventually resembled that seen in bronchitic patients with CO_2 insensitivity and retention. The findings suggest a central action of propranolol.

INDEX: Propranolol, Ventilation, Human.

AUTHORS: Neil-Dwyer, G.

TITLE: The Clinical Importance of Lipid Solubility in Beta Blockers.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 52, pp. 19-22, 1981.

DRUGS: Propranolol (80 mg, b.i.d.), Metoprolol (200 mg/d), Exprenolol (160 mg/d), and Atenolol (100 mg/d)

SUBJECTS: 12 patients (10 with either anterior or middle cerebral arterial aneurysms; 9 received beta-blocker therapy, 8 had sustained a subarachoid hemorrhage 1 week prior)

PROCEDURES: ECG analysis.

FINDINGS:
In a series of studies involving patients who had suffered sub-arachnoid hemorrhage (SAH), urinary catecholamines and plasma cortisol levels were found to be significantly elevated. Certain abnormal ECG changes (peaked P-wave, short P-R interval, long QTCs [Q-T intervals corrected for heart rate] and large U-wave) were found to be correlated with very high catecholamine levels; most of these probably resulted from beta adrenergic activity, as they could be reversed with propranolol. Additionally, it was clear that if a patient sustained three to four of the ECG changes, the prognosis was poor. A subsequent study looked at the effect of propranolol on morbidity and mortality in patients with SAH. All patients treated with propranolol improved significantly during the first day of admission and generally had normal ECGs whereas controls continued to evidence abnormal ECGs.

INDEX: Propranolol, Metoprolol, Exprenolol, Atenolol, Biochemistry, HR, Human.

AUTHORS: Nolan, B. T.

TITLE: Acute Suicidal Depression Associated with the Use of Timolol.

REFERENCE: Journal of the American Medical Association, Vol. 247, p. 1563, 1982.

DRUGS: Timolol

SUBJECTS: One 65-year-old woman

PROCEDURES: Case History

FINDINGS:
Timolol was one of several medications she was taking to reduce intraocular pressure. The association between drug use and the psychiatric symptoms (acute suicidal depression) cannot be conclusively proved. The clear association of symptoms with the timing of medication usage, together with the known propensity of the beta-blocker to produce similar symptoms, provides strong circumstantial evidence.

INDEX: Timolol, Psychology, Human.

AUTHORS: Pardridge, W. M., Sakiyama, R., and Fierer, G.

TITLE: Blood-brain Barrier Transport and Brain Sequestration of Propranolol and Lidocaine.

REFERENCE: American Journal of Physiology, Vol. 247, pp. 582-588, 1984.

DRUGS: 3H-Propranolol, 14C-Butanol, and 14C-Lidocaine

SUBJECTS: Rat brain studies, in vivo

PROCEDURES: The study was designed to characterize the kinetics of drug transport and sequestration in rat brain, in vivo, using the carotid injection technique.

FINDINGS:
Both propranolol and lidocaine are sequestered by the brain, and the half time of clearance from the brain to blood was 6-7 min. The t1/2 of propranolol association and dissociation reactions with the brain sequestration system are 0.38 + 0.03 and 1.33 + 0.20 min, respectively. The blood brain barrier transport of propranolol and lidocaine was inhibited by an acidic pH, and drug transport was mediated by a low-affinity, high-capacity saturable transport system.

INDEX: Propranolol, Butunol, Lidocaine, Histology, Nonhuman.

AUTHORS: Peters, N. L., Anderson, K. C., Reid, P. R., and Taylor, G. J.

TITLE: Acute Mental Status Changes Caused by Propranolol.

REFERENCE: Johns Hopkins Medical Journal, Vol. 143, p. 163, 1978.

DRUGS: Propranolol (10 mg every 6 h)

SUBJECTS: One 74-year-old black woman was admitted for control of episodic palpitations

PROCEDURES: Case history and observation by attending physician(s).

FINDINGS:
The woman had mild dementia, became disoriented, and developed paranoid delusions when treated with a low dose of propranolol. There was no evidence of cardiovascular instability, and the symptoms resolved within a week. Rechallenge with propranolol led to a recurrence of mental status changes. The article discusses other similar case studies.

INDEX: Propranolol, Psychology, HR, Human.

870

AUTHORS: Peterson, E. S., Whipp, B. J., Davis, J. A., Huntsman, D. J., Brown, H. V., and Wasserman, K.

TITLE: Effects of Beta-adrenergic Blockade on Ventilation and Gas Exchange During Exercise in Humans.

REFERENCE: Journal of Applied Physiology, Vol. 54, pp. 1306-1313, 1983.

DRUGS: Propranolol (0.2 mg/kg, i.v.)

SUBJECTS: 6 healthy young males

PROCEDURES: Exercise using a bicycle ergometer. Inspired and expired PO_2 and PCO2 were measured for each breath. Electrocardiogram was monitored continously.

FINDINGS:
Heart rate during exercise decreased about 20%, and cardiac output decreased about 15%. The relation between work rate and O_2 uptake (VO_2) was unaffected, whereas maximal O_2 uptake (VO_2, max) decreased about 5%, and the anaerobic threshold, estimated non-invasively, was lowered 23%. Beta-blockade was associated with a significantly increased time constant for VO_2 but had no change in VCO_2 and Ve.

INDEX: Propranolol, Exercise, Ventilation, HR, Human.

880

AUTHORS: Prichard, B. N. C.

TITLE: Beta Blockade and the Effects of Stress on the Normal and Ischaemic Heart.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 52, pp. 9-18, 1981.

DRUGS: Isoprenaline
Labetalolol (10, 40, and 160 mg)
Propranolol (10 mg)

SUBJECTS: Post-infarction patients
Patients with angina pectoris

PROCEDURES: Review paper.

FINDINGS:
The article discusses evidence that beta blocking drugs are useful in angina pectoris, inhibiting the tachycardia of exercise and other forms of stress, such as emotion. In myocardial infarction, there is experimental evidence in animals and man for the effectiveness of these drugs in restoring the supply/demand balance of the ischemic areas, thus limiting infarct size. The drugs may act partly by redistributing the coronary blood flow from areas of relatively good perfusion to those less well supplied. Cardiac pain is reduced in angina and also post-infarction. Muscle contraction of the ischemic myocardium may be improved. Beta-adrenergic blocking drugs may reduce the incidence of reinfarction when given prophylactically.

INDEX: Propranolol, Isoprenaline, Labetalol, Review, Human.

890

AUTHORS: Ratey, J. J., Morrill, R., and Oxenkrug, G.

TITLE: Use of Propranolol for Provoked and Unprovoked Episodes of Rage.

REFERENCE: American Journal of Psychiatry, Vol. 140, pp. 1356-1357, 1983.

DRUGS: Clinical doses of propranolol.

SUBJECTS: Three case reports: 42-year-old female, 49-year-old female, and 24-year-old male

PROCEDURES: Case history.

FINDINGS:
The authors report three cases indicating that propranolol may be effective in the treatment of overall aggressiveness in brain-damaged or mentally retarded patients.

INDEX: Propranolol, Psychology, Human.

900

AUTHORS: Richardson, J. S., Stacey, P. D., Russo, N. J., and Musty, R. E.

TITLE: Effects of Systemic Administration of Propranolol on the Timing Behavior (DRL-20) of Rats.

REFERENCE: Archives Internationales de Pharmacodynamie et de Therapie, Vol. 197, pp. 66-71, 1972.

DRUGS: Propranolol (0.5-25.0 mg/kg, i.p.)

SUBJECTS: Rats

PROCEDURES: Rats were placed on an operant conditioning schedule requiring them to bar-press based on the passage of time.

FINDINGS:
Injections of propranolol disrupted the performance in a way that closely parallels the effects of amygdaloid ablation. Previous reports have linked the amygdala in the production of both depression and anxiety. These findings may, in some part, explain the clinical reports that propranolol is associated with psychotic depression in cardiac patients.

INDEX: Propranolol, Psychology, Nonhuman.

910

AUTHORS: Russell, J. W. and Schuckit, M. A.

TITLE: Anxiety and Depression in Patient on Nadolol.

REFERENCE: Lancet, Vol. 2, p. 1268, 1982.

DRUGS: Nadolol (80 mg)

SUBJECTS: One 35-year-old man

PROCEDURES: Case study

FINDINGS:
Within 2 days of an increase in dosage of his medication, the patient fell into servere depression without having had any previous history of psychiatric distrubance.

INDEX: Nadolol, Psychology, Human.

920

AUTHORS: Sable, D. L., Brammell, H. L., Sheehan, M. W., Nies, A. S., Gerber, J., and Horwitz, L. D.

TITLE: Attenuation of Exercise Conditioning by Beta-adrenergic Blockade.

REFERENCE: Circulation, Vol. 65, pp. 679-684, 1982.

DRUGS: Propranolol (Plasma concentrations were 100-292 ng/ml)

SUBJECTS: 17 male volunteers, ages 21-35

PROCEDURES: ECGs were recorded. Oxygen consumption was calculated. Vital capacity and expired air over the first second of forced expiration (FEV1) were measured on a Stead-Well Spirometer. Exercise was performed using a Quinton Treadmill. Blood pressure was measured by sphygmomanometry. Gases were analyzed by Beckman LB-2.

FINDINGS:
Subjects who received propranolol had only modest improvement in exercise duration and no significant change in maximal oxygen uptake. With training, diastolic pressure at maximal exercise was unchanged in subjects who received propranolol. It was concluded that high levels of propranolol markedly attentuate aerobic conditioning in normal subjects.

INDEX: Propranolol, HR, Ventilaton, BP, Biochemistry, Exercise, Human.

930

AUTHORS: Safta, L., Kory, B., Cuparencu, B., and Ilea, F.

TITLE: Interaction of Propranolol with Some Analgesics.

REFERENCE: Physiologie, Vol. 17, pp. 247-250, 1980.

DRUGS: Propranolol (5-20 mg/kg, i.p.)
Levomepromazine (2.5-5.0 mg/kg, i.p.)
Morphine (5-20 mg/kg, s.c.)

SUBJECTS: Mice of both sexes, weighing approximately 25 g

PROCEDURES: The period between administrations of the above drugs and of the tested opiate was 20 min. In one group, 30 min post drug, Haffner's procedure for assessing the level of pain was performed and repeated every 20 min until 110 min had elapsed. In another group, the pain stimulation test was administered 30 min after morphine, and repeated every 30 min for a total of 150 min.

FINDINGS:
As expected, morphine produced a potent dose-related analgesia. Propranolol with morphine potentiated the effect but not significantly. Propranolol by itself did not produce an analgesic effect. Levomepromazine demonstrated a low dose-related analgesia effect. By combining the two drugs, a potentiation of analgesia occurred but was not statistically significant.

INDEX: Propranolol, Levomepromazine, Morphine, Cutaneous, Human.

940

AUTHORS: Salem, S. A. M. and McDevitt, D. G.

TITLE: Central Effects of Single Oral Doses of Propranolol in Man.

REFERENCE: British Journal of Clinical Pharmacology, Vol. 17, pp. 31-36, 1984.

DRUGS: Propranolol (40, 80, 160, 320 mg)

SUBJECTS: 6 healthy male volunteers, ages 22-34

PROCEDURES: Central drug effects were assessed using two-flash fusion threshold (2 FFT), simple reaction time (SRT), Digital Copying Test (DCT), Symbol Digit Modalities Test (SDMT), Gibson Spiral Maze Test (GSMT), and mood rating scales for tension, alertness, depression, detachment and anxiety.

FINDINGS:
Two-flash fusion threshold was prolonged by 40-, 80-, or 160-mg doses of propranolol but not by 320 mg (largest effect was with 40 mg at post 3 h). The SRTs were prolonged by all doses; DCT was reduced by 40-, 80-, and 320-mg doses but not by 160 mg. The drug reduced the expected retest increase for the SDMT at all doses except 320 mg. Mood scales demonstrated increased detachment with the low dose and decreased alertness with the 80- and 320-mg doses.

INDEX: Propranolol, Complex Performance, Vision, Psychology, Human.

950

AUTHORS: Savaki, H. E., Kadekaro, M., Jehle, J., and Sokoloff, L.

TITLE: Alpha- and Beta-adrenoreceptor Blockers Have Opposite Effects on Energy Metabolism of the Central Auditory System.

REFERENCE: Nature, Vol. 276, pp. 521-523, 1978.

DRUGS: dl-Propranolol (0.25, 0.5, or 0.85 mg/kg)
Phentolamine (0.25, 0.5, or 0.85 mg/kg)

SUBJECTS: Male rats (350-400 g)

PROCEDURES: Autoradiographic 14C-deoxyglucose assay has made it possible to measure the local rates of glucose utilization (LCGU).

FINDINGS:
Pulse rate declined; body temperature tended to fall by as much as $2^{O}C$; and arterial PCO_2 and PO_2 tended to rise with propranolol. During the administration of propranolol, all animals showed a gradual decline in alertness and responsiveness to tactile and auditory stimulation. Propranolol produced a dose-dependent decrease in local cerebral structures and exhibited statistically significant reductions in glucose utilization. At the highest dosage (1mg/kg/min), glucose utilization was significantly depressed in all but 2 of the 26 structures examined.

INDEX: Propranolol, Phentolamine, Biochemistry, Histology, HR, Ventilation, Cutaneous, Auditory, Nonhuman.

960

AUTHORS: Schwartz, S., Davies, S., and Juers, J. A.

TITLE: Life-threatening Cold and Exercise-Induced Asthma Potentiated by Administration of Propranolol.

REFERENCE: Chest, Vol. 78, pp. 100-101, 1980.

DRUGS: Propranolol (40 mg three times per day)

SUBJECTS: Two case reports: (1) 63-year-old man who smoked and had essential hypertension; and (2) 47-year-old man with essential hypertension.

PROCEDURES: Case histories.

FINDINGS:
Both patients were brought to the emergency room cyanotic and diaphoretic with no breath sounds. In both cases, the men were working in cold areas and were on propranolol. Both responded favorably to aminophylline, i.v., and oxygen.

INDEX: Propranolol, Heat Stress, Human.

970

AUTHORS: Scott, D.

TITLE: Another Beta-blocker Causing Eye Symptoms.

REFERENCE: British Medical Journal, Vol. 2, p. 1221, 1977.

DRUGS: Metoprolol (100-200 mg)

SUBJECTS: One female patient

PROCEDURES: Case history.

FINDINGS:
Patient reported pain and soreness in both eyes following metropolol. The drug was withdrawn, and the symptoms abated. She was then put on another beta-blocker, and the symptoms returned. Her eyes became so dry that she had trouble opening her lids.

INDEX: Metoprolol, Vision, Human.

980

AUTHORS: Shander, R. and Greenblatt, D.

TITLE: Propranolol's Psychiatric Side Effects.

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 3, p. 65, 1983.

DRUGS: Propranolol

SUBJECTS: 394 hypertensive patients

PROCEDURES: Review paper.

FINDINGS:
The author hypothesizes that more lipophilic (lipid soluble) beta-blockers have a greater propensity to produce central effects than do relatively less lipophilic beta-blockers.

INDEX: Propranolol, Review, Human.

990

AUTHORS: Shapiro, A., Kimchi, A., Rob, J. L., Gotsman, M. S., and Lewis, B. S.

TITLE: Ocular Effects of Acebutolol and Propranolol.

REFERENCE: Metabolic, Pediatric and Systemic Ophthalmology, Vol. 4, pp. 87-88, 1980.

DRUGS: Acebutolol (600-1200 mg)
Propranolol (120-240 mg)

SUBJECTS: 14 patients suffering from angina pectoris

PROCEDURES: Random double-blind design. Subjects were examined for visual acuity, Schirmer Test No. 1, break-up time of tear film, and intraocular pressure.

FINDINGS:
Acebutolol produced smaller changes than propranolol in measurements of tear secretion. There was no difference in visual acuity and intraocular pressure comparing the two drugs.

INDEX: Propranolol, Acebutolol, Vision, Human.

1000

AUTHORS: Sheehan, M. W., Brammell, H. L., Sable, D. L. Niles, A. S., and Horwitz, L.D.

TITLE: Effect of Beta-adrenergic Blockade on Circulating Catecolamines and Dopamine-beta-hydroxylase Activity During Exercise in Normal Subjects.

REFERENCE: American Heart Journal, Vol. 105, pp. 777-782, 1983.

DRUGS: Propranolol (160-320 mg/day in four equal doses)

SUBJECTS: 9 normal nonhypertensive subjects, ages 22-34

PROCEDURES: Radioenzymatic assay measurement of norepinephrine and epinephrine. Measurements were made at rest, at 30% max isometric handgrip exercise (IHE), and during submax and max dynamic treadmill exercise. Also measured dopamine-beta-hydroxylase (DBH).

FINDINGS:
The study concluded that competitive blockade of beta-adrenergic receptors at the tissue level does not alter neural release of norepinephrine or DBH and has little effect on adrenal release of epinephrine.

INDEX: Propranolol, Exercise, Biochemistry, Human.

1010

AUTHORS: Shopsin, B., Hirsch, J., and Gershon, S.

TITLE: Visual Hallucinations and Propranolol.

REFERENCE: Biological Psychiatry, Vol. 10, pp. 105-107, 1975.

DRUGS: Propranolol (40 mg, single dose)

SUBJECTS: One acute hospitalized schizophrenic

PROCEDURES: Patient observation.

FINDINGS:
Schizophrenic patient had a minor visual hallucination after a single dose of propranolol. Within 2.5 h the phenomenon had disappeared.

INDEX: Propranolol, Vision, Psychology, Human.

1020

AUTHORS: Singh, K. P., Bhandari, D. S., and Mahawar, M. M.

TITLE: Effects of Propranolol (A Beta Adrenergic Blocking Agent) On Some Central Nervous System Parameters.

REFERENCE: Indian Journal of Medical Research, Vol. 59, pp. 786-794, 1971.

DRUGS: Propranolol (0.25, 0.5, and 1.0 mg/kg, i.p.)

SUBJECTS: Mice

PROCEDURES: Tested for drug influence on barbiturate hypnosis, analgesia, anticonvulsant effect, metrazol convulsions, strychnine convulsions, audiogenic seizure test, perphenazine-induced catatonia, nicotine-induced tremors, effect on motor activity, effect on body temperature, and influence on conditioned avoidance behavior.

FINDINGS:
Propranolol increased the hypnosis caused by pentobarbital. The drug had no effect on the righting reflex. Propranolol did not display any analgesic effects. The drug had no effect on the different stages of convulsion induced by shock (electrically or chemically induced). All phases of convulsions were blocked in audiogenic seizures. Propranolol delayed the onset of perphenazine catatonia and decreased the intensity. It produced a marked reduction of nicotine-induced tremors. General motor activity and amphetamine hyperactivity were reduced. Propranolol produced significant lowering of the rectal temperature and decreased amphetamine-induced hyperthermia. Beta-blockade had no effect on the conditioned avoidance response.

INDEX: Propranolol, Neuroelectric, Cutaneous, Musculoskeletal, Temperature, Complex Performance, Auditory, Nonhuman.

1030

AUTHORS: Sjoberg, H., Frankenhaeuser, M., and Bjurstedt, H.

TITLE: Interactions Between Heart Rate, Psychomotor Performance and Perceived Effort During Physical Work as Influenced by Beta-adrenergic Blockade.

REFERENCE: Biological Psychiatry, Vol. 8, pp. 31-43, 1979.

DRUGS: Propranolol (0.25 mg/kg)

SUBJECTS: 15 healthy male subjects

PROCEDURES: Three reaction-time tasks were performed while the subjects were pedaling at five different work loads on a bicycle ergometer.

FINDINGS:
After injection of propranolol, there was the usual reduction in heart rate and an increase in catecholamine excretion. There was no significant drug effect on the reaction-time tasks.

INDEX: Propranolol, Exercise, Complex Performance, HR, Biochemistry, Human.

1040

AUTHORS: Sklar, J., Johnston, G. D., Overline, P., Gerber, J. G., and Brammell, H. L.

TITLE: The Effects of a Cardioselective (Metoprolol) and a Non-selective (Propranolol) Beta-adrenergic Blocker on the Response to Dynamic Exercise in Normal Men.

REFERENCE: Circulation, Vol. 65, pp. 894-899, 1982.

DRUGS: Propranolol (40-80 mg every 6 hr)
Metoprolol (100 mg every 6 hr)

SUBJECTS: 10 healthy active male volunteers

PROCEDURES: Dynamic treadmill exercise to exhaustion. Heart rate, arterial pressure, oxygen consumption, minute ventilation, and CO_2 production were monitored.

FINDINGS:
Wide variations in plasma drug levels after a given oral dose were noted. Both drugs attenuated heart rate and systolic blood pressure responses to exercise. Neither drug affected diastolic blood pressure, maximum oxygen consumption, max minute ventilation, or the anaerobic threshold. There was no evidence that the cardioselective drug metoprolol is superior to propranolol in terms of the ability to perform or respond to short-term max exercise.

INDEX: Propranolol, Metoprolol, Exercise, HR, BP, Ventilation, Human.

1050

AUTHORS: Sleight, P.

TITLE: Clinical Use of Beta-blockers in Hypertension.

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 52, pp. 3-8, 1981.

DRUGS: Thiazides and beta-blockers in general

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
Reviews of beta-blockers in the treatment of mild hypertension. This form of antihypertensive therapy can produce a protective influence against cerebrovascular events and reduce fatal and nonfatal rate of myocardial infarction. The comparative efficacy and side effects profile of the various clinically available beta-blockers are discussed. The degree of water or lipid solubility may determine the rate of penetration of brain tissue with attendant central nervous system effects.

INDEX: Review, Human.

1060

AUTHORS: Smith, D. L. and Looney, T. J.

TITLE: Seizures Secondary to Thyrotoxicosis and High-dosage Propranolol Therapy.

REFERENCE: Archives of Neurology, Vol. 40, pp. 457-548, 1983.

DRUGS: Propranolol (2,640 mg/day)
(This is a very large daily dose!)

SUBJECTS: One 18 year-old man in basic training

PROCEDURES: Case history.

FINDINGS:
The initial physical exam demonstrated a resting tachycardia of 140 beats/min, a fine upper-extremity tremor, and a diffuse goiter of 100 g. Neurologic exam was normal except for generalized hyperreflexia. Patient had high T3 and T4 levels and the patient suffered episodes of paroxysmal atrial fibrillation. Propranolol hydrochloride therapy was instituted. There were no adverse effects until 2 weeks later when the patient experienced a series of three seizures. The dose of propranolol was reduced to 960 mg/day, and finally the patient was treated only with iodine and thyroid replacement, and he remained seizure-free.

INDEX: Propranolol, HR, Musculoskeletal, Neuroelectric, Human.

1070

AUTHORS: Smits, J. F. M., Van Essen, H., and Struyker-Boudier, H. A. J.

TITLE: Is the Antihypertensive Effect of Propranolol Caused by an Action Within the Central Nervous System?

REFERENCE: Journal of Pharmacology and Experimental Therapeutics, Vol. 215, pp. 221-225, 1980.

DRUGS: Propranolol (0.01-5.0 mg/kg/d, intracerebral ventricular (i.c.v.)

SUBJECTS: Hypertensive rats

PROCEDURES: Ventricular catheters were surgically placed for the i.c.v. administration of propranolol. Blood pressure was measured via an indwelling catheter in the abdominal aorta. Osmotic minipumps were used for the i.c.v. infusion.

FINDINGS:
It was concluded that in conscious hypertensive rats, propranolol does not lower blood pressure through a direct action within the CNS. Earlier reports of such a central effect may have been artifacts of the experimental techniques used by others and have probably resulted from aspecific actions of the drug. The authors recommend that attention be paid to peripheral actions like reduced cardiac output and possible intrarenal effects to explain the long-term antihypertensive actions of the drug.

INDEX: Propranolol, BP, Nonhuman.

1080

AUTHORS: Smulyan, H. and Eich, R. H.

TITLE: Effect of Beta Sympathetic Blockade on the Initial Hemodynamic Response to Exercise.

REFERENCE: Journal of Laboratory and Clinical Medicine, Vol. 71, pp. 378-389, 1968.

DRUGS: Propranolol (approx. 0.3 mg/kg)

SUBJECTS: 22 dogs

PROCEDURES: Cardiac output was measured by an undescribed technique. Administration and sampling catheters were inserted into the jugular vein and the femoral artery. The dogs were trained to stand quietly with a snug-fitting veterinary mask over the mouth and nose and then to walk on a treadmill at 1.25 mph at a 10% grade.

FINDINGS:
This investigation demonstrated that the influence of the beta-adrenergic receptor system on the initial hemodynamic response to exercise primarily affects cardiac output and peripheral resistance rather than heart rate, blood pressure, or oxygen consumption. The changes in heart rate were sufficiently variable such that the calculated stroke volumes were not significantly reduced by propranolol except at rest and following 90 s of exercise. This study shows that despite beta-adrenergic blockade, the circulation maintains a qualitatively normal response to exercise (the cardiac output and heart rate rise promptly and overshoot with the onset of exertion). Although incomplete beta-adrenergic blockade cannot be excluded completely, the doses of propranolol used have been associated with attenuation of reflex beta- sympathetic responses. Therefore, all exercise changes mediated through this system should have been similarly attenuated.

INDEX: Propranolol, Exercise, HR, Biochemistry, BP, Ventilation, Nonhuman.

1090

AUTHORS: Sponsel, W. E., Dallas, N. L., and Burbridge, L.

TITLE: Visual Field Survival: The Response to Timolol Therapy in Open-Angle Glaucoma.

REFERENCE: British Journal of Ophthalmology, Vol. 67, pp. 220-227, 1983.

DRUGS: Timolol

SUBJECTS: 36 patients with open-angle glaucoma

PROCEDURES: Intraocular pressure (IOP) was measured by applanation tonometery. Visual field assessment was determined by routine Goldmann perimetry. Quanitative approximations of total field areas were obtained from Goldmann traces using mathematical means.

FINDINGS:
Tonometric monitoring of IOP indicated that timolol therapy reduced IOP 24.3-34.5%. Sixty three percent of those treated, who were monitored for field survival, showed significant field loss. Statistical analysis indicated that field survival measurement was a more accurate clinical guide to the progress of glaucoma than IOP monitoring.

INDEX: Timolol, Vision, Human.

1100

AUTHORS: Srivastava, B. N., Dwiveli, R. B., Rao, V. S. C., and Mehta, G. S.

TITLE: Effect of Beta-blockers in Lung Functions.

REFERENCE: Journal of the Association of Physicians of India, Vol. 22, pp. 723-727, 1974.

DRUGS: Propranolol (10 mg)
Pindolol (2.5 mg)

SUBJECTS: 24 cases of classical angina, ages 26-27

PROCEDURES: Spirometry was done in a sitting position. Measurements included forced vital capacity, timed vital capacity, max voluntary ventilation, max breathing capacity, inspiratory reserve volume, expiratory reserve volume, and breath-holding time.

FINDINGS:
A reduction in forced vital capacity was seen after propranolol. There was no change with pindolol. Neither drug produced a significant drop in forced expiratory volume. Neither drug remarkably changed inspiratory reserve volume nor expiratory reserve volume. Propranolol produced a slight reduction in maximum voluntary ventilation; however, pindolol produced a slight increase. Breath holding time was decreased by propranolol but not affected by pindolol.

INDEX: Propranolol, Pindolol, Ventilation, Human.

1110

AUTHORS: Stephen, S. A.

TITLE: Unwanted Effects of Propranolol.

REFERENCE: American Journal of Cardiology, Vol. 18, pp. 463-472, 1966.

DRUGS: Propranolol

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
The article discusses common types of side effects (visual disturbances, purpura, paresthesias, and mental confusion); effects relating to the pharmacologic action of propranolol (hypotension, bradycardia, cardiac failure, heart block, dyspnea and wheezing); biochemical abnormalities (blood count, blood urea, serum transaminase); and death during propranolol therapy. The incidence of side effects is low; when they do occur, they are of a transient nature. Marked deviations from normal biochemical values are uncommom and revert to normal when propranolol is stopped. There is no evidence to suggest that propranolol causes renal or hepatic disease. The most important group of unwanted effects relate to those due to the pharmacologic action of the drug, e.g., hypotension and heart failure. These occur in patients whose hearts are so severely diseased that heart failure is imminent. When patients have been previously digitalized, such effects are uncommon. Bradycardia, when it occurs, is likely to be due to unopposed vagal activity and has been shown to respond to atropine, i.v.

INDEX: Propranolol, Review, Human.

1120

AUTHORS: Sternberg, D. B., Gold, P. E., and McGaugh, J. L.

TITLE: Memory Facilitation and Impairment with Supraseizure Electrical Brain Stimulation: Attenuation with Pretrial Propranolol Injections.

REFERENCE: Behavioral and Neural Biology, Vol. 38, pp. 261-268, 1983.

DRUGS: Propranolol (0.5 mg/kg, i.p.)

SUBJECTS: Rats (90-days-old)

PROCEDURES: The effects of post-training stimulation (supraseizure) of the frontal areas of the cortex on the retention (memory) of active avoidance (low footshock) or high footshock.

FINDINGS:
Propranolol did not affect retention peformance in the nonstimulated groups. With high footshock, the propranolol group demonstrated good memory performance. With low footshock, both propranolol and saline groups demonstrated diminished retention. Pretreatment with propranolol resulted in reduction of memory facilitation and amnesia.

INDEX: Propranolol, Complex Performance, Neuroelectric, Stress, Nonhuman.

1130

AUTHORS: Stone, W. N., Gleser, G. C., and Gottschalk, L. A.

TITLE: Anxiety and Beta-adrenergic Blockade.

REFERENCE: Archives of General Psychiatry, Vol. 29, pp. 620-622, 1973.

DRUGS: Propranolol (60 mg)

SUBJECTS: 24 healthy male volunteers

PROCEDURES: Doses given orally 12 h preceding testing; speech analysis, stress interview, and plasma free fatty acid determinations.

FINDINGS:
As a group, those subjects receiving propranolol had significantly lower initial anxiety. A stress interview was followed by increases of anxiety scores to comparable levels in both groups. Plasma free fatty acid determinations did not differ significantly. Pulse rate at the end of the 55-min session was significantly lower for the propranolol group. There was a positive correlation for the control group and an inverse correlation for the propranolol group between anxiety (as measured from speech) and free fatty acids.

INDEX: Propranolol, Auditory, Stress, Biochemistry, Complex Performance, Human.

1140

AUTHORS: Svedenhag, J., Henriksson, J., and Juhlin-Dannfelt, A.

TITLE: Beta-adrenergic Blockade and Training in Human Subjects: Effects on Muscle Metabolic Capacity.

REFERENCE: American Journal of Physiology, Vol. 247, pp. 305-311, 1984.

DRUGS: Propranolol (160 mg/day)

SUBJECTS: 16 male subjects, ages 20-31

PROCEDURES: Subjects trained for 8 weeks on cycle ergometers. Eight were treated during the training period with propranolol. Muscle biopsy specimens were analyzed; VO_2 max was determined; subjects completed a submax cycle ergometer test; and heart rate was monitored.

FINDINGS:
Training-induced increases in VO_2 max and decreases in blood lactate and norepinephrine concentrations at submax exercise were not different between the two groups. The activity of the mitochrondrial enzymes citrate synthase (CS), succinate dehydrogenase (SDH), cytochrome c oxidase (Cyt-c-ox), and 3-hydroxyacyl-CoA dehydrogenase (HAD) in the muscle increased significantly with training (drug group, +47, +33, +38, and 22%; placebo group, +75, +70, +87, and 63%, respectively). Cyt-c-ox and HAD increased significantly more in the placebo group, while a tendency to increase was noted for SDH. Muscle capillary density increased (+17, +19%) with training in the two groups.

INDEX: Propranolol, Exercise, Histology, Ventilation, HR, Human.

AUTHORS: Tartara, A., Bo, P., Savoldi, F., Arrigo, A., and Moglia, A.

TITLE: Experimental EEG Study on Central Effects of Propranolol.

REFERENCE: IL Farmaco, Vol. 31, pp. 574-579, 1976.

DRUGS: Propranolol (3-6 mg/kg, i.v., or i.c.)

SUBJECTS: Rabbits

PROCEDURES: Deep brain electrodes were placed in the motor cortex, sensory-motor cortex, visual cortex, medial and lateral nuclei of the thalamus, midbrain reticular formation, and the posterolateral hypothalamus. ECG was recorded concurrently.

FINDINGS:
Pulse rate dropped by 23%. A "synchronization" of electric cortical activity occurred. Spindle activity increased by 40%. Arousal time for vibroacoustic stimuli was reduced by 30%. Propranolol reduced the arousal reaction in reticular stimulation (increased voltage needed) and increased the high-frequency threshold in the hypothalamus.

INDEX: Propranolol, Neuroelectric, HR, Auditory, Nonhuman.

AUTHORS: Tattersfield, A. E., Leaver, D. G., and Pride, N. B.

TITLE: Effects of Beta-adrenergic Blockade and Stimulation on Normal Human Airways.

REFERENCE: Journal of Applied Physiology, Vol. 35, pp. 613-619, 1973.

DRUGS: Propranolol (20 mg, i.v.)
Salbutamol (inhaled)

SUBJECTS: 6 healthy physicians (1 female and 5 males), ages 28-39

PROCEDURES: Venous blood was taken for estimation of plasma propranolol by fluorometric method. Forced expiratory volume and vital capacity were measured with a dry spirometer. Total lung capacity was determined by measuring thoracic gas volume in a constant volume plethysmograph. Mean airway resistance was also measured.

FINDINGS:
No changes were observed in airway conductance, lung volume, maximum or partial expiratory flow volume curves, expiratory static pressure volume curves, or dynamic lung compliance. There was a small increase in inspiratory static lung recoil pressures, but this was not statistically significant. Four of the subjects were also studied before and after beta-adrenergic stimulation with inhaled salbutamol. Airways conductance rose in three of the subjects indicating the presence of resting bronchomotor tone. The study concluded that there were no effects on larger airways and probably no effects on the smaller airways with propranolol for these subjects.

INDEX: Propranolol, Salbutamol, Biochemistry, Ventilation, Human.

1170

AUTHORS: Taylor, E. A. and Turner, P.

TITLE: Propranolol in Experimentally Induced Stress.

REFERENCE: British Journal of Psychiatry, Vol. 139, pp. 545-549, 1981.

DRUGS: Propranolol (80 mg)

SUBJECTS: 12 healthy volunteers (4 men and 8 women), ages 20-23

PROCEDURES: The influence of propranolol on exercise (sustained right leg extension) was assessed by measures of heart rate, blood pressure, and skin temperature.

FINDINGS:
Propranolol significantly reduced heart rate before the stress, at the end of the stress period, and after the stress. It increased heart rate during stress, systolic BP, and warming of skin of the trunk. Cooling of skin on the hand and diastolic BP did not change.

INDEX: Propranolol, Exercise, HR, BP, Temperature, Human.

1180

AUTHORS: Twentyman, O. P., Disley, A., Gribbin, H. R., Alberti, K. G. M. M., and Tattersfield, A. E.

TITLE: Effect of Beta-adrenergic Blockade on Respiratory and Metabolic Responses to Exercise.

REFERENCE: Journal of Applied Physiology, Vol. 51, pp. 788-793, 1981.

DRUGS: Propranolol (80 mg)

SUBJECTS: 16 fit, non-obese male, medical students, ages 20-30

PROCEDURES: Used the cycle ergometer. Analysis included heart rate (HR), ventilation (Ve), CO_2 output (VCO_2), and O_2 uptake (VO_2). Drug metabolites were measured.

FINDINGS:
Propranolol reduced HR in all studies and endurance time during progressive exercise. During constant-work-rate exercise, the changes with propranolol depended on time and work rate. At 50% max, VO_2, VCO_2, and Ve were reduced in early exercise but had returned to normal by 5 min. At 70% max, VO_2 and VCO_2 were lower initially with propranolol but then rose more rapidly. By minute 5, Ve was greater with propranolol, coinciding with a rapidly rising venous lactate, and VCO_2. The resulting increase in anerobic metabolism during heavy exercise would explain the increased Ve at 5 min. The metabolic findings are consistant with the predominant muscle energy source being glycogen. Propranolol may also alter VO_2 and VCO_2 by changing the metabolic substrates for exercise. Reduced lipolysis from beta-adrenergic blockade may account for various enzymatic changes relating to energy for the exercising muscle.

INDEX: Propranolol, Exercise, HR, Ventilation, Biochemistry, Human.

1190

AUTHORS: Tyrer, P. J. and Lader, M. H.

TITLE: Response to Propranolol and Diazepam in Somatic and Psychic Anxiety.

REFERENCE: British Medical Journal, Vol. 2, pp. 14-16, 1974.

DRUGS: Propranolol (40 mg, 3-9 times/day)
Diazepam (2 mg, 3-9 times/day)

SUBJECTS: 12 chronic psychiatric outpatients

PROCEDURES: Patients were treated for 1 week using a balanced crossover experimental design. The degree of anxiety was rated in each patient by a modification of the Hamilton rating scale in which 100 mm linear scales were used instead of categorical ones. Clinical subjective evaluations were made by both patient and physician.

FINDINGS:
Propranolol was more effective than placebo in patients with somatic anxiety but not in those with psychic anxiety. The authors suggested that propranolol should be reserved for patients whose anxiety symptoms are mainly somatic. The results indicate that diazepam is better at relieving morbid anxiety.

INDEX: Propranolol, Diazepam, Psychology, Human.

1200

AUTHORS: van Herwaarden, C. L. A., Binkhorst, R. A., Fennis, J. F. M., and van 'T Laar, A.

TITLE: Effects of Propranolol and Metoprolol on Haemodynamic and Respiratory Indices and on Perceived Exertion.

REFERENCE: British Heart Journal, Vol. 41, pp. 99-105, 1979.

DRUGS: Propranolol (80 mg 2 times/day)
Metoprolol (100 mg 3 times/day)

SUBJECTS: 8 men with untreated essential hypertension

PROCEDURES: Exercise was performed in the sitting position on a bicycle ergometer. The expiratory peak flow rate was measured before and after 6 min of exercise. Expired gases (CO_2 and O_2) were monitored. Blood pressure was measured noninvasively.[2] An EKG was recorded every minute.

FINDINGS:
Both beta-blockers resulted in reduced heart rate, cardiac output, and blood pressure, however, stroke volume increased. Total peripheral resistance did not change. During exercise, the expiratory peak flow increased equally in every period. The peak flow rate at rest, as well as during exercise, was reduced by propranolol, while metoprolol had no influence. Neither of the two drugs changed O_2 consumption, CO_2 production, tidal volume, respiratory rate or perceived exertion.[2]

INDEX: Propranolol, Metoprolol, Exercise, Ventilation, BP, HR, Human.

1210

AUTHORS: Weber, J. C. P.

TITLE: Beta-adrenoreceptor Antagonists and Diplopia.

REFERENCE: Lancet, Vol. 2, p. 1047, 1982.

DRUGS: Propranolol

SUBJECTS: NA

PROCEDURES: Review paper.

FINDINGS:
The adverse reactions register of the Committee on Safety of Medicines contains 9495 reports of adverse reactions to beta-adrenoreceptors. In twenty-four of these reports, diplopia was considered to be related to the drug. Positive regression of the diplopia with discontinuance of the drug occurred in 14 of these cases.

INDEX: Propranolol, Vision, Review, Human.

1220

AUTHORS: Williams, F. M., Singh, B. N., Ambler, P. K., and Dorrington, R.

TITLE: The Effects of Propranolol, Practolol, and Metoprolol on Exercise-Induced Tachycardia in Relation to Plasma Levels in Man.

REFERENCE: Clinical and Experimental Pharmacology and Physiology, Vol. 3, pp. 473-482, 1976.

DRUGS: Propranolol (80 mg)
Practolol (250 mg)
Metoprolol (100 mg)

SUBJECTS: 6 healthy male volunteers, ages 25-52

PROCEDURES: Exercise monitored with ECG.

FINDINGS:
Between 1.5 and 2 h post-administration, propranolol reduced the exercise-induced tachycardia by 27%, practolol reduced it 28%, and metoprolol reduced it 30%. Resting heart rates were significantly reduced by propranolol and metoprolol but not by practolol. Other studies have reported metoprolol to have less bronchospastic effects in patients with airway obstruction. The potentially serious oculocutaneous side effects encountered during prolonged practolol therapy would possibly indicate that the role of an alternative beta blocker, such as metoprolol, may merit investigation.

INDEX: Propranolol, Practolol, Metoprolol, Exercise, HR, Human.

1230

AUTHORS: Yates, D.

TITLE: Syncope and Visual Hallucinations, Apparently From Timolol.

REFERENCE: Journal of the American Medical Association, Vol. 244, p. 768, 1980.

DRUGS: Timolol

SUBJECTS: One 78-year-old female with open-angle glaucoma

PROCEDURES: Case history.

FINDINGS:
Patient experienced confusion, inability to speak or write for a few minutes, and vivid and frightening hallucinations for several days. The timolol was stopped, and the hallucinations ceased within a few hours and did not recur.

INDEX: Timolol, Vision, Psychology, Human.

1240

AUTHORS: Yudofsky, S. C., Stevens, L., Silver, J., Barsa, J., and Williams, D.

TITLE: Propranolol in the Treatment of Rage and Violent Behavior Associated with Korsakoff's Psychosis.

REFERENCE: American Journal of Psychiatry, Vol. 141, pp. 114-115, 1984.

DRUGS: Propranolol (600 mg/day)

SUBJECTS: One 40-year-old male with a 20-year history of alcohol abuse

PROCEDURES: Case report and discussion: Propranolol was phased-in with haloperidol and finally replaced by it.

FINDINGS:
Two weeks after the 600-mg dose was reached, Mr. A's rage attacks were markedly reduced, and restraints were no longer necessary. Stimuli that would have normally provoked a rage episode did not. Mr. A's hallucinations diminished, however, he remained disoriented.

INDEX: Propranolol, Psychology, Human.

Acebutolol	160,990
ACh	10
Alcohol	420,750
Amylobarbitone	170
Atenolol	410,550,560,610,830
Atropine	10,20,70,280,500
Auditory	50,160,670,950,1020,1130,1150
Biochemistry	40,110,300,310,360,380,390,520,530,540,580, 590,620,710,720,740,770,830,920,950,1000,1030, 1080,1130,1160,1180
BP(blood pressure)	30,40,50,60,70,80,90,130,150,190,200,270,290,300, 320,330,360,480,520,570,590,620,640,650,680,690,710,720, 750,760,780,790,920,1040,1070,1080,1170,1200
Bunitrolol	200,760
Butanol	850
Captopril	330

Chlorpromazine	570
Complex Performance	160,170,180,290,380,410,520,600,670,680,750,940, 1020,1030,1120,1130
Cutaneous	930,950,1020
Diazepam	1190
Epinephrine	150,370
Eserine	10
Exercise	30,40,60,70,80,90,100,130,210,280,320,330,360,390, 440,460,480,520,530,540,560,580,590,610,620,690,710,720, 760,770,780,790,870,920,1000,1030,1040,1080,1140,1170, 1180,1200,1220
Exprenolol	830
G-Tolerance	130
Heat Stress	200,570,640,960
Histamine	150
Histology	10,210,250,310,460,700,730,850,950,1140
HR (heart rate)	30,40,50,60,70,80,90,100,130,140,150,190,200,270, 280,290,320,330,360,380,390,470,480,520,530,560,570,590, 620,640,650,670,680,690,710,720,730,750,760,770,780,790, 830,860,870,920,950,1030,1040,1060,1080,1140,1150,1170, 1180,1200,1220

Human	20,30,40,50,60,70,80,90,100,120,130,140,150,160,170 180,190,200,210,220,230,240,250,260,270,280,290,300, 310,320,330,340,350,360,370,380,390,400,410,420,430, 440,450,470,480,490,510,520,530,540,550,560,580,590, 600,610,620,630,650,660,670,680,690,710,720,740,750, 760,770,780,790,800,810,820,830,840,860,870,880,890, 910,920,930,940,960,970,980,990,1000,1010,1030,1040, 1050,1060,1090,1100,1110,1130,1140,1160,1170,1180, 1190,1200,1210,1220,1230,1240
Hydrochlorothiazide	300
Isoprenaline	880
Isoproterenol	150
Labetalol	880
Levomepromazine	930
Lidocaine	850
Methyldopa	90
Methysergide	570
Metoprolol	40,50,100,250,270,300,350,360,440,480,520,540,550,560, 830,970,,1040,1200,1220
Morphine	930
Musculoskeletal	670,680,750,1020,1060
Nadolol	550,910

Neuroelectric	380,670,1020,1060,1120,1150
Nonhuman	10,110,310,460,500,570,640,700,730,850,900,950, 1020,1070,1080,1120,1150
Norepinephrine	150
Oxprenolol	120
Penbutolol	80,180
Pharmacology	370,420,800
Phentolamine	950
Pindolol	340,550,1100
Practolol	1220
Propranolol	10,20,30,40,50,60,70,80,90,100,110,120,130,140,150 160,170,180,190,210,220,230,240,250,260,270,280,290, 300,310,320,330,340,350,370,380,390,400,410,420,430, 440,450,460,470,480,490,500,510,520,530,540,550,560, 570,580,590,600,610,620,640,650,670,680,690,700,710, 720,730,740,750,770,780,790,800,810,820,830,850,860, 870,880,890,900,920,930,940,950,960,980,990,1000,1010, 1020,1030,1040,1060,1070,1080,1100,1110,1120,1130,1140, 1150,1160,1170,1180,1190,1200,1210,1220,1240

Psychology	240,340,400,430,470,490,510,650,670,680,840,860,890, 900,910,940,1010,1190,1230,1240,
Questionnaire	120,260,680
Review	220,230,410,550,630,800,880,980,1050,1110,1210
Salbutamol	1160
Sotalol	10,340,410,670
Stress	270,320,470,600,650,690,730,1120,1130
Sweating	20,380
Temperature	1020,1170
Timolol	620,660,840,1090,1230
Tolamolol	60
Tripolidine	730
Ventilation	100,140,190,280,350,360,530,540,560,590,640,690,760,790, 820,870,920,950,1040,1080,1100,1140,1160,1180,1200
Vision	10,160,260,340,450,660,680,940,970,990,1010,1090 1210,1230